Human cortex development is shaped by molecular and cellular brain systems

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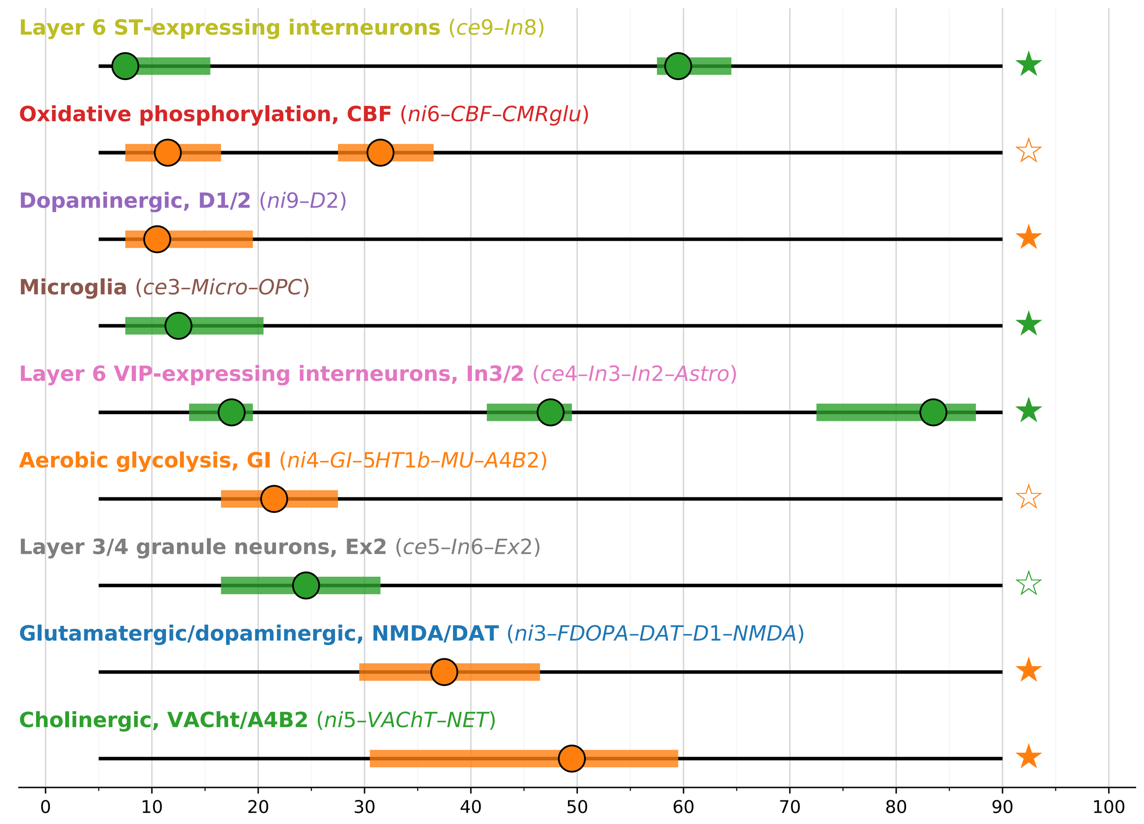
Research motivation & impact

- Human cerebral cortex morphology is subject to complex and diverse changes over the lifespan[1,2].
- Several factors might influence cortical thickness (CT) development and maturation, but human data are scarce.
- Through spatial correlation approaches[3,4], recent advances in normative modeling of population-scale neuroimaging data[1,2], and availability of multi-level atlases of molecular and cellular brain systems[5–7], we identify potential mechanisms underlying human CT development.
- This work…
  1) provides new hypotheses on mechanisms involved in human cortex development,
  2) introduces a framework for studying neurodevelopmental mechanisms in vivo on the individual level, promising new insights into typical and atypical neurodevelopment alike, and
  3) further emphasizes the value of normative modeling frameworks in neurodevelopmental research.

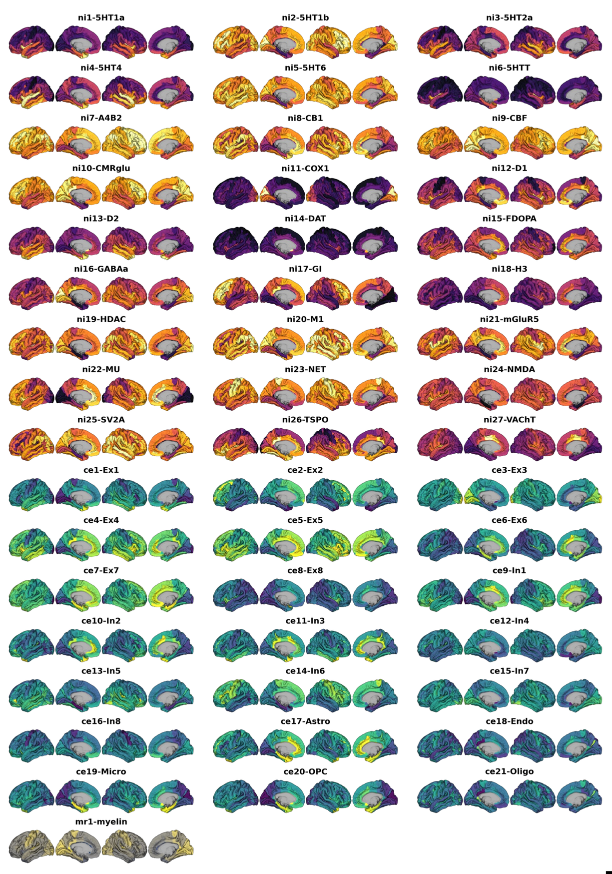
Results overview



Data sources

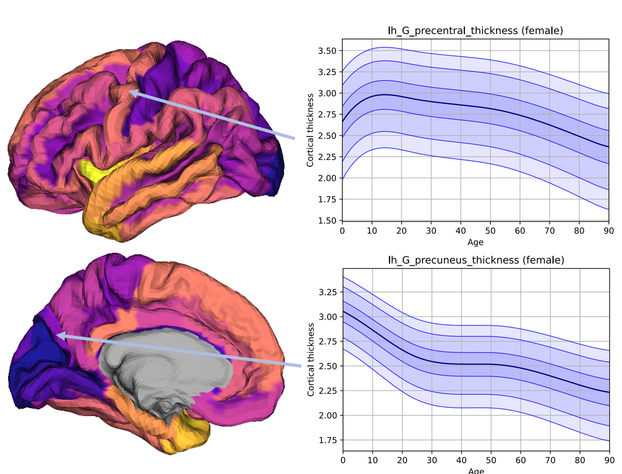
"Multilevel" maps of molecular and cellular brain systems[5–7]

(n = 49, nuclear imaging, ABA, MRI)



Normative models of "representative" CT development[2]

(n = 58,836; ~2 to 100 years; 148 regions)



ABCD longitudinal CT data[8]

(n = 6,789; ~10 and 12 years)

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IMAGEN longitudinal CT data[9]

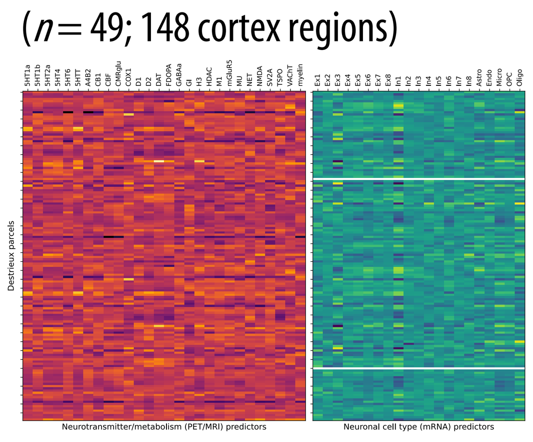
(n = 995 to 1,278; ~14, 19, and 22 years)

imagen

Data processing

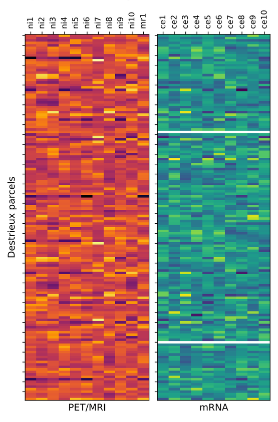
Parcellation

(n = 49; 148 cortex regions)



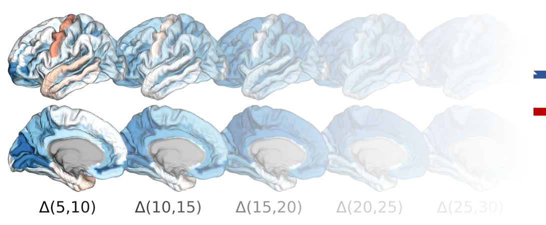
Dimensionality reduction

(n = 21; factor analysis)



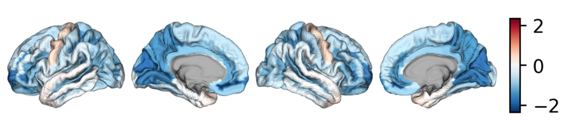
Timestep-wise CT change

(sliding window, 5-year-steps)

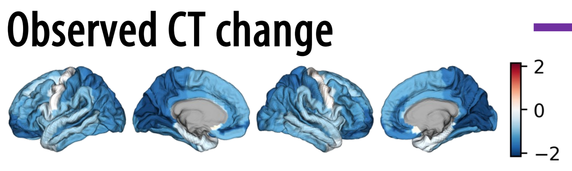


Subject-wise:

Predicted CT change



Observed CT change



Spatial correlation[10]
(CT)

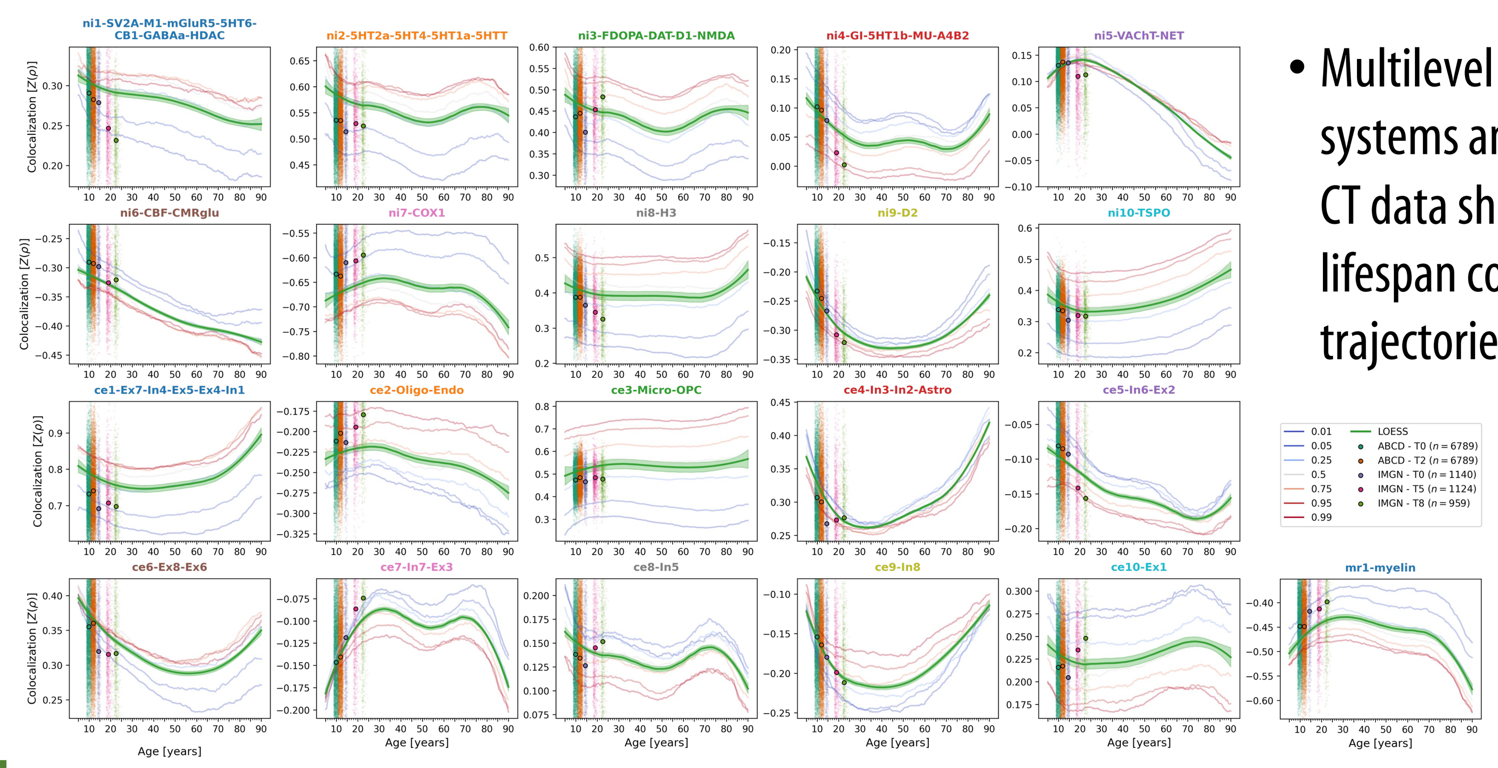
Regression analysis[10]
(CT change)

Dominance analysis[10]
(CT change)

Regression & Dominance analysis[10]
(CT change)

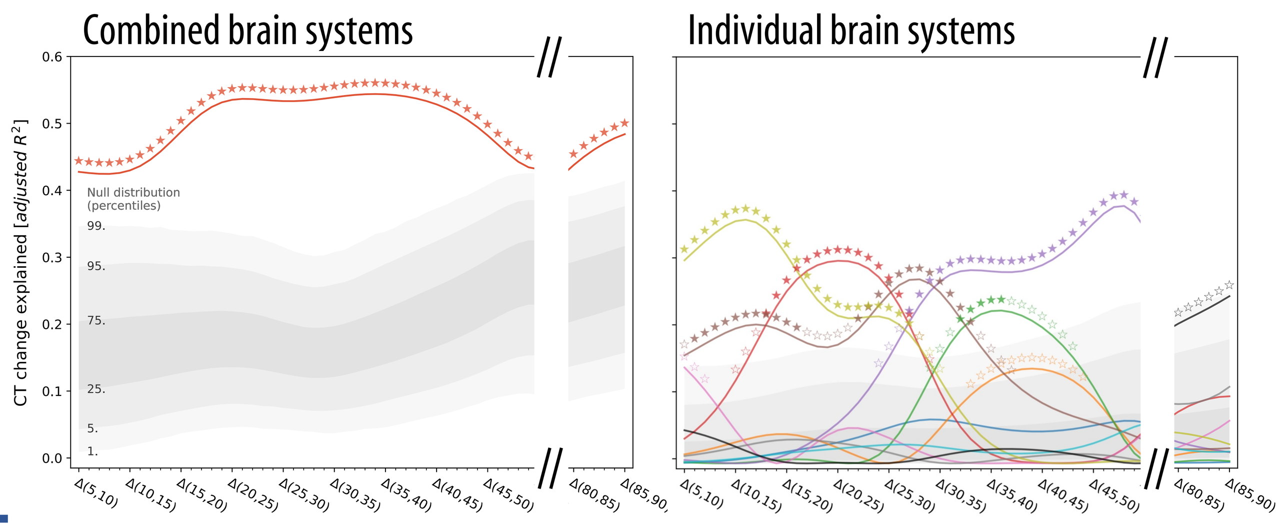
Analyses & results

How do spatial colocalization patterns develop across the lifespan?



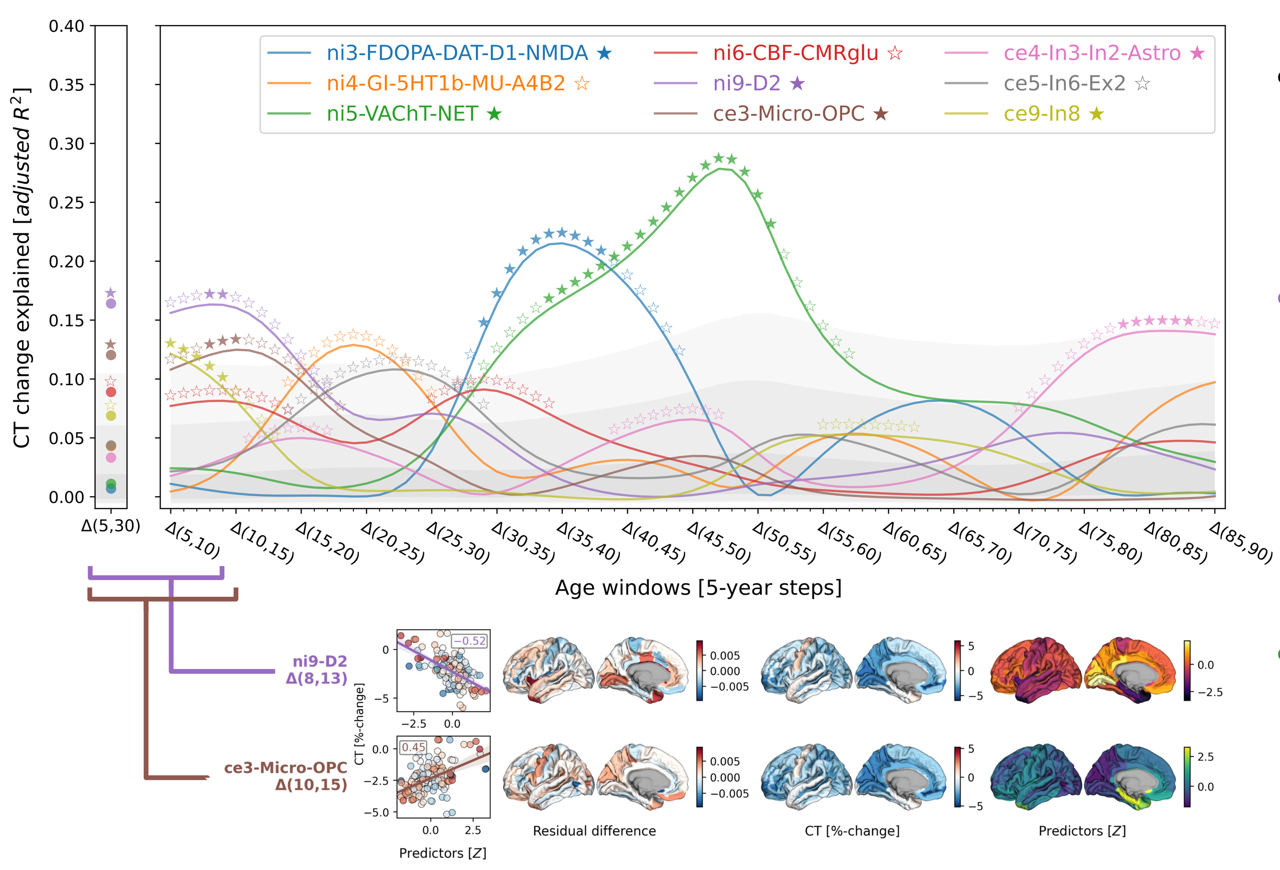
- Multilevel brain systems and modeled CT data show diverse lifespan colocalization trajectories.

To what extent can multilevel brain systems explain patterns of cortical development?



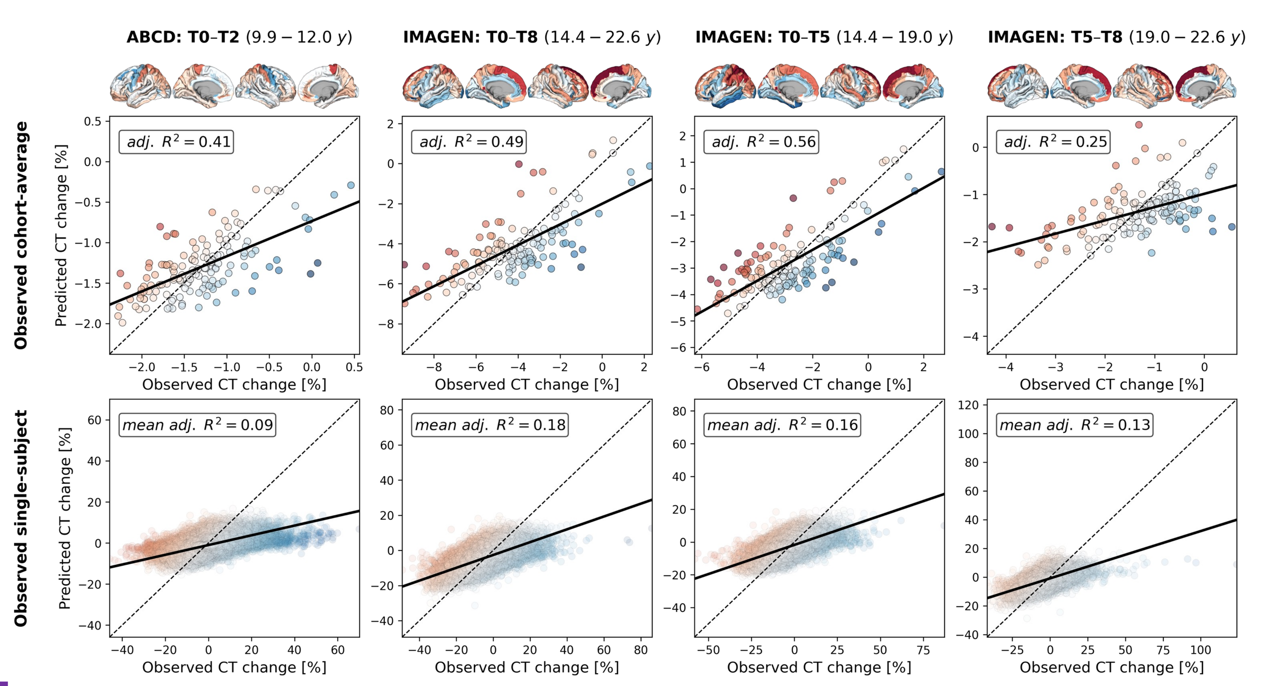
- Molecular (Fig.) and cellular systems explain up to 55% of modeled lifespan CT change.
- Individual systems explain up to 40%.

Which brain systems and cortex regions are most relevant across developmental stages?



- Only 9 systems can explain up to 57% of modeled CT change.
- D1/2 dopaminergic receptors, microglia, ST interneurons, and brain metabolism explain early CT development.
- Cholinergic and glutamatergic receptors explain later CT change.

Do the observed association patterns replicate in single-subject longitudinal data?



- Modeled results replicate in independent longitudinal data.
- 6 biological systems explain up to 59% of cohort-average and 18% of single-subject CT development.

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