Human cortex development is shaped by molecular and cellular brain systems

Leon D. Lotter[1,2,3], Amin Saberi[1,2,4], Justine Y. Hansen[5], Bratislav Misic[5], Casey Paquola[1], Gareth J. Barker[6], Arun L. W. Bokde[7], Sylvane Desrivières[8], Herta Flor[9,10], Antoine Grigis[11], Hugh Garavan[12], Penny Gowland[13], Andreas Heinz[14], Rüdiger Brühl[15], Jean-Luc Martinot[16], Marie-Laure Paillère[16,17], Eric Artiges[16,18], Dimitri Papadopoulos Orfanos[11], Tomáš Paus[19,20], Luise Poustka[21], Sarah Hohmann[22], Juliane H. Fröhner[23], Michael N. Smolka[23], Nilakshi Vaidya[24], Henrik Walter[14], Robert Whelan[25], Gunter Schumann[24, 26], IMAGEN Consortium, Frauke Nees[9,22,27], Tobias Banaschewski[22], Simon B. Eickhoff[1,2], and Juergen Dukart[1,2]

[1]INM-7: Brain and Behaviour, Research Centre Jülich, Germany | [2]Institute of Systems Neuroscience, Heinrich-Heine-Universität Düsseldorf, Germany | [3]Max Planck School of Cognition, Leipzig, Germany | [4-27] see QR code

HEINRICH HEINE UNIVERSITÄT DÜSSELDORF
SYSTEMS NEUROSCIENCE

MAX PLANCK SCHOOL of cognition

JÜLICH Forschungszentrum

Brain & Behaviour

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l.lotter@fz-juelich.de

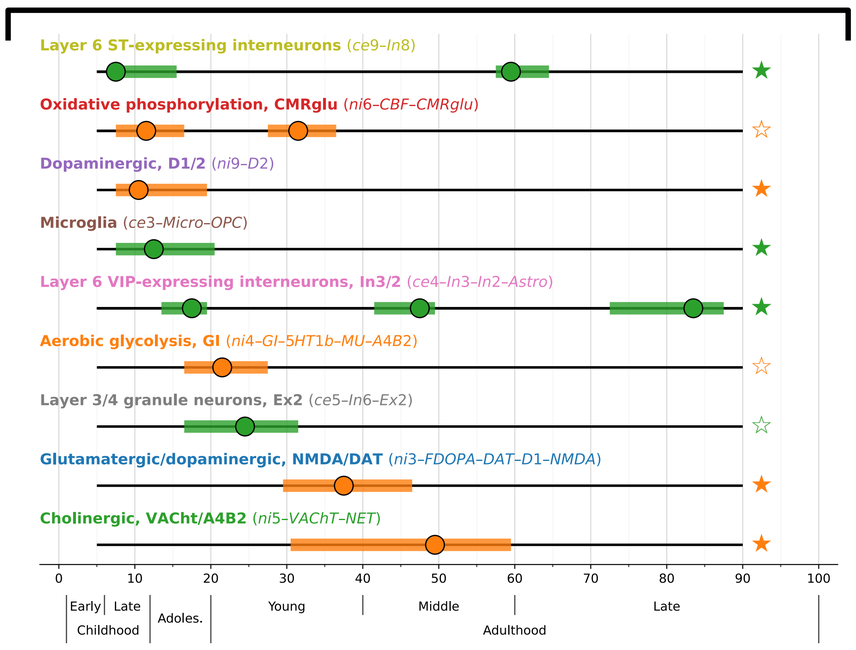
LeonDLotter

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 lifespan changes, 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 brain atlases covering a wide range of neural cell populations and neurobiological processes[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.

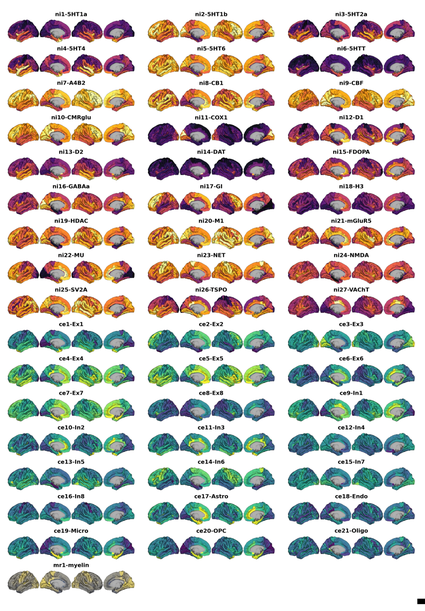
Results overview



Data sources

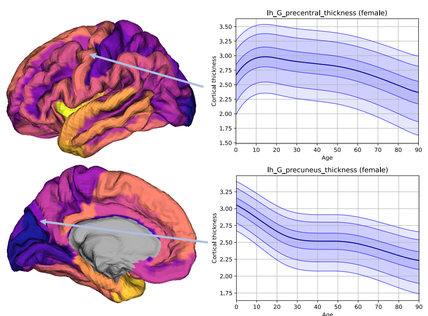
Atlases of molecular and cellular "neurobiological markers"[5–7]

(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)

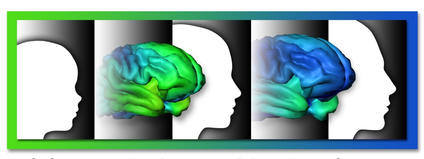


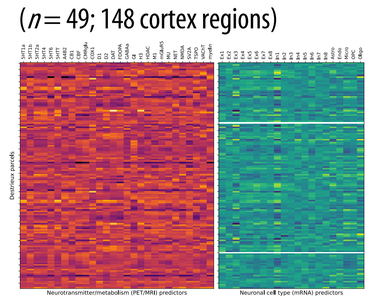
IMAGEN longitudinal CT data[9]

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

Data processing

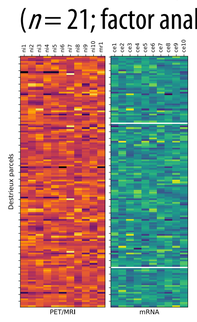
Parcellation

(n = 49; 148 cortex regions)



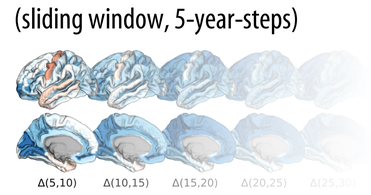
Dimensionality reduction

(n = 21; factor analysis)

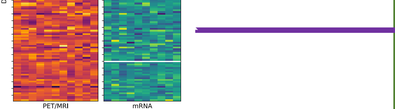


Timestep-wise CT change

(sliding window, 5-year-steps)



Subject-wise: Predicted CT change

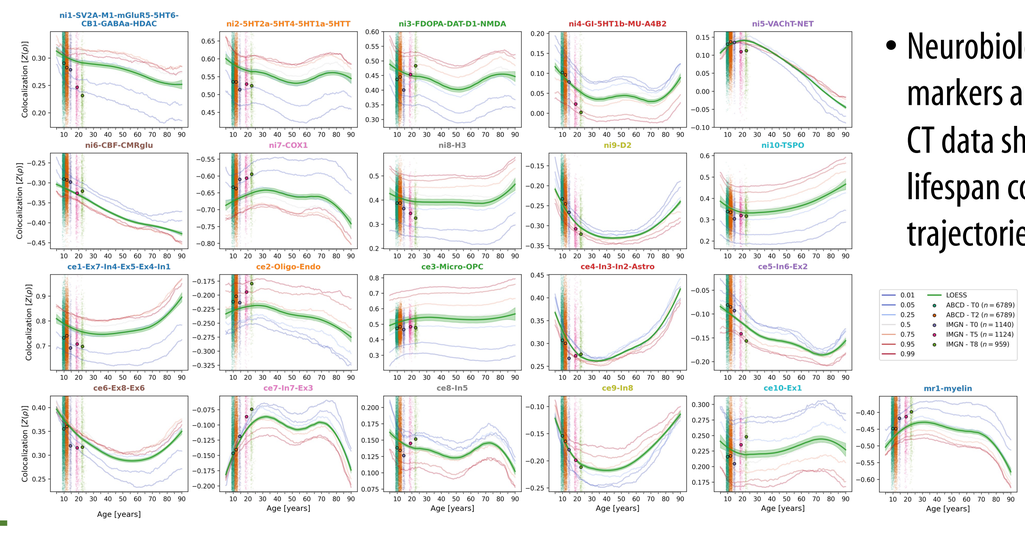


Observed CT change

Analyses & results

Spatial correlation[10] (CT)

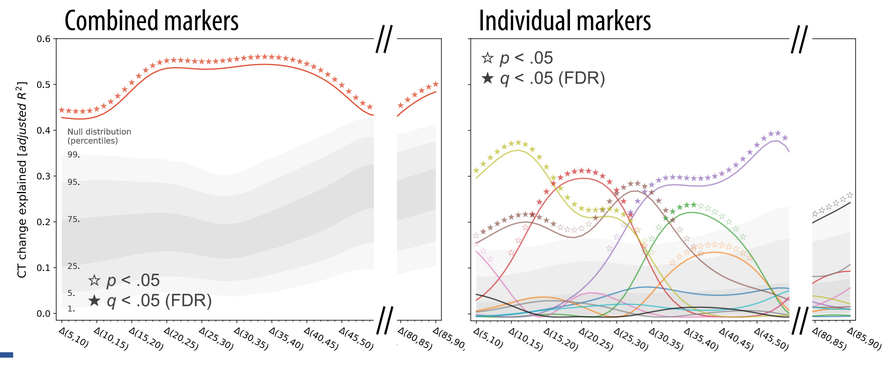
How do spatial colocalization patterns develop across the lifespan?



- Neurobiological markers and modeled CT data show diverse lifespan colocalization trajectories.

Regression analysis[10] (CT change)

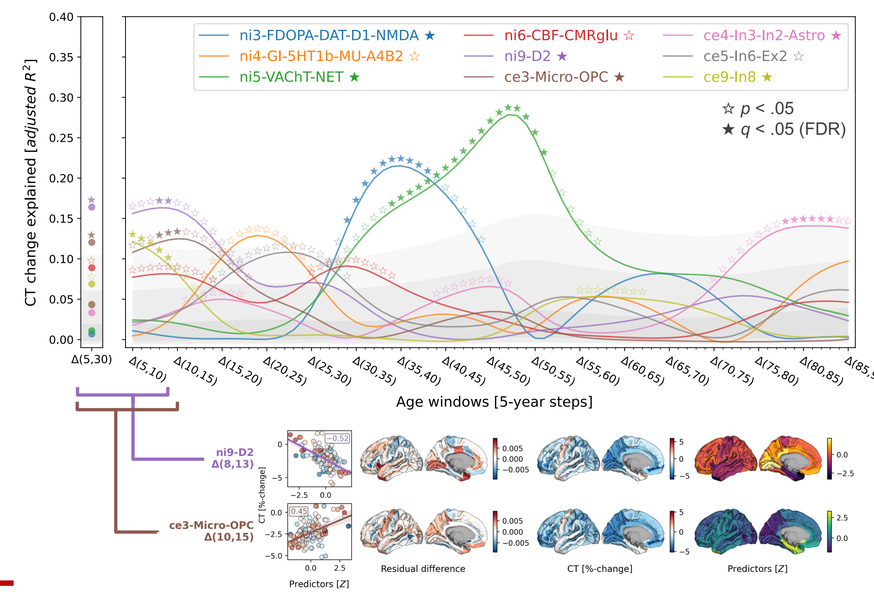
To what extent can neurobiological markers explain patterns of cortical development?



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

Dominance analysis[10] (CT change)

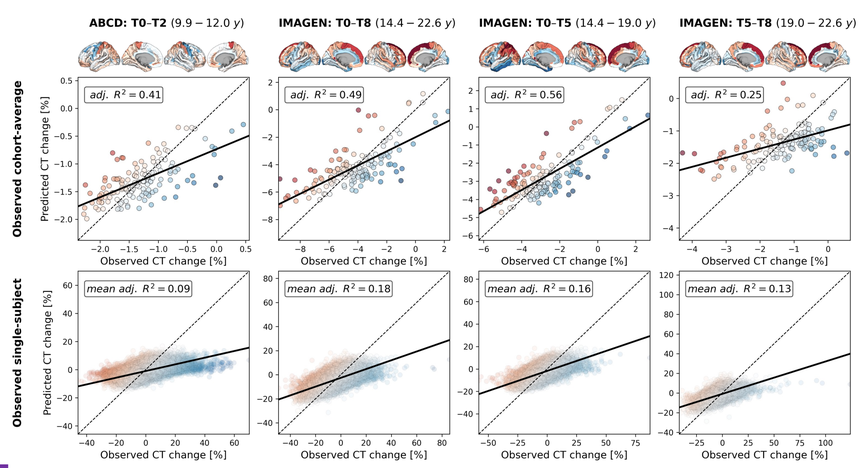
Which markers and cortex regions are most relevant across developmental stages?



- Only 9 markers 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.

Regression & Dominance analysis[10] (CT change)

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



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

[1] Bethlehem, R. A. I. et al. (2022). Brain charts for the human lifespan. *Nature, 604*(7906), Article 7906
[2] Rutherford, S. et al. (2022). Charting brain growth and aging at high spatial precision. *eLife, 11*, e72904.
[3] Dukart, J. et al. (2021). JuSpace: A tool for spatial correlation analyses of magnetic resonance imaging data with nuclear imaging derived neurotransmitter maps. *Hum. Brain Mapp., 42*(3), 555–566.
[4] Vidal-Pineiro, D., et al. (2020). Cellular correlates of cortical thinning throughout the lifespan. *Sci. Rep., 10*(1), Article 1.
[5] Hansen, J.Y. et al. (2022). Mapping neurotransmitter systems to the structural and functional organization of the human neocortex. *Nat. Neurosci., 25*, 1569–1581.
[6] Hawrylycz, M.J. et al. (2012). An anatomically comprehensive atlas of the adult human brain transcriptome. *Nature, 489*(7416), 391–399.
[7] Lake, B.B. et al. (2016). Neuronal subtypes and diversity revealed by single-nucleus RNA sequencing of the human brain. *Science, 352*(6293), 1586–1590.
[8] Casey, B.J. et al. (2018). The Adolescent Brain Cognitive Development (ABCD) study: Imaging acquisition across 21 sites. *Dev. Cogn. Neuro., 32*, 43–54.
[9] Schumann, G. et al. (2010). The IMAGEN study: Reinforcement-related behaviour in normal brain function and psychopathology. *Mol. Psychiatry, 15*(12), Article 12.
[10] Lotter, L.D. and Dukart, J. (2022). JuSpyce - a toolbox for flexible assessment of spatial associations between brain maps. *Zenodo.*