Translating time across humans and model organisms from transcriptional and structural variation

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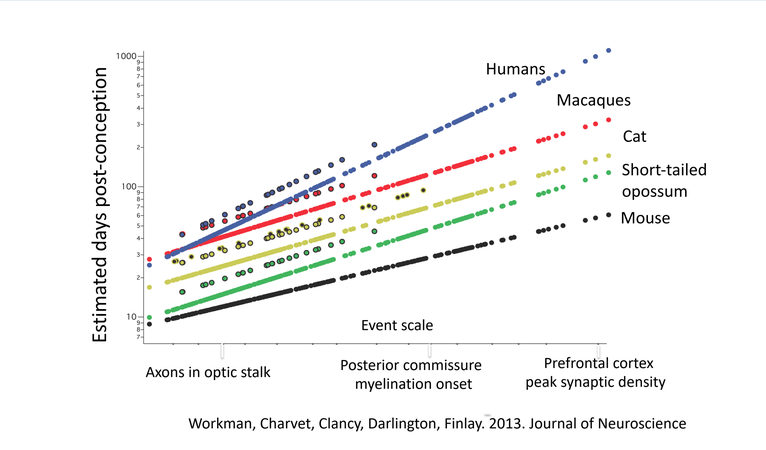
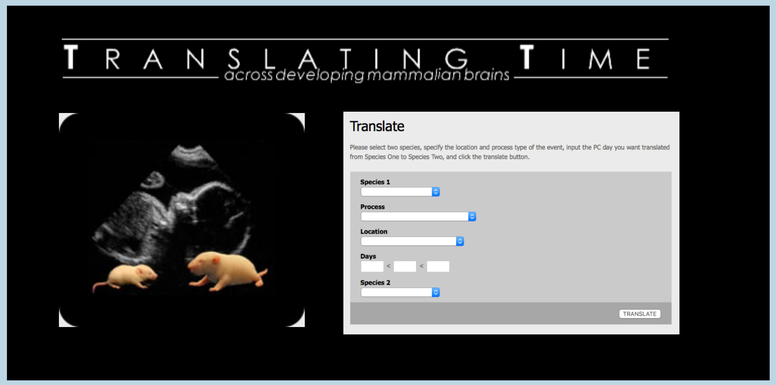
1) The timing of rapid transformations serves to identify corresponding ages across species



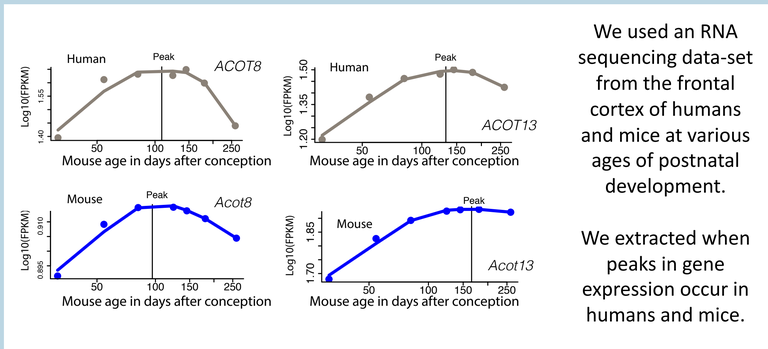
Workman, Charvet, Clancy, Darlington, Finlay. 2013. Journal of Neuroscience

2) Translatingtime.org identifies corresponding time points across species during fetal ages



Questions: Can temporal variation in transcription be used to identify corresponding ages across species?

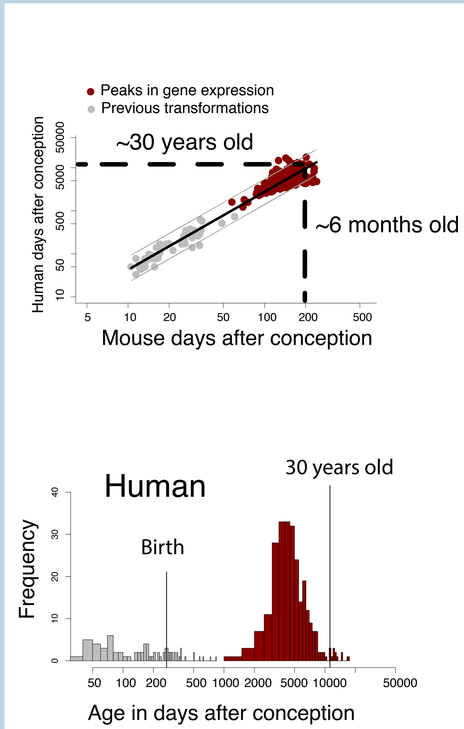
3) Capturing temporal variation in transcription to find corresponding ages across humans and mice

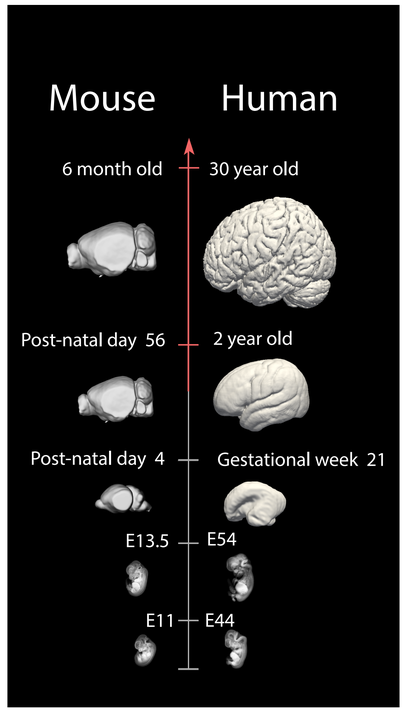


We used an RNA sequencing data-set from the frontal cortex of humans and mice at various ages of postnatal development.

We extracted when peaks in gene expression occur in humans and mice.

4) Temporal variation in transcription identifies corresponding ages up to 30 years of age in humans and ~6 months old mice



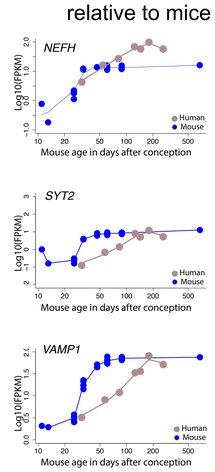


Examples of equivalent ages in humans and mice

5) Temporal profiles of genes linked to neurons that project over long distances in the cortex (i.e., supragranular-enriched genes) are protracted in humans relative to mice

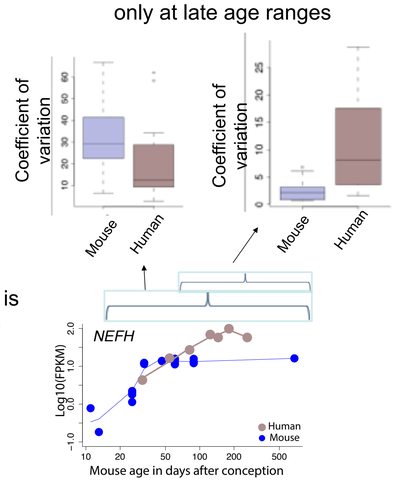
Supragranular-enriched genes (n=19) are linked to long-range projections in the cortex

The temporal profiles of some of these genes appear protracted in humans relative to mice

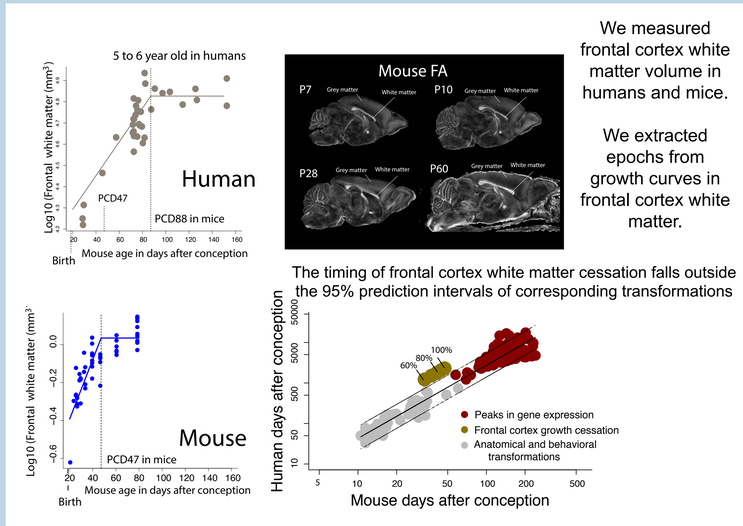


Age in humans is mapped onto mouse

The coefficient of variation is significantly greater in humans only at late age ranges



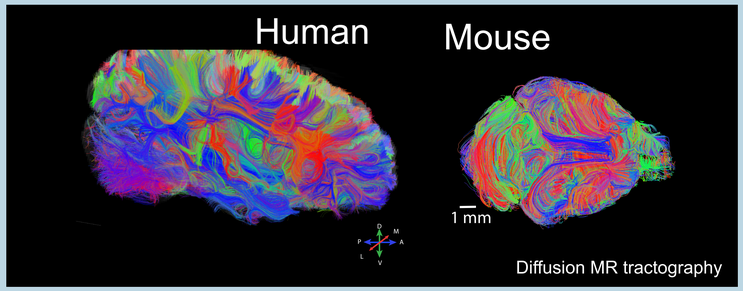
6) The cortex white matter (which contains long-range projections) is protracted in humans versus mice



We measured frontal cortex white matter volume in humans and mice.

We extracted epochs from growth curves in frontal cortex white matter.

7) We are using diffusion MR tractography to identify the impact of protracted development on the evolution of connections.



Significance

Temporal variation in transcription:
- -identifies corresponding ages at postnatal ages in humans and mice.
- -variation in the developmental timetable of connectivity across species

These findings are available:

Hendy JP, Takahashi E, van der Kouwe AJ, Charvet CJ. 2019. Brain wiring and supragranular-enriched genes linked to protracted human frontal cortex development. BioRxiv. https://doi.org/10.1101/746248.

Translating time across species:
www.translatingtime.net

Acknowledgements

The RNA sequencing data-set is from Lister R, Mukamel EA, Nery JR, Urich M, Puddifoot CA, Johnson ND, et al. Global epigenomic reconfiguration during mammalian brain development. *Science* 2013; 341(6146): 1237905. doi: 10.1126/science.1237905.