

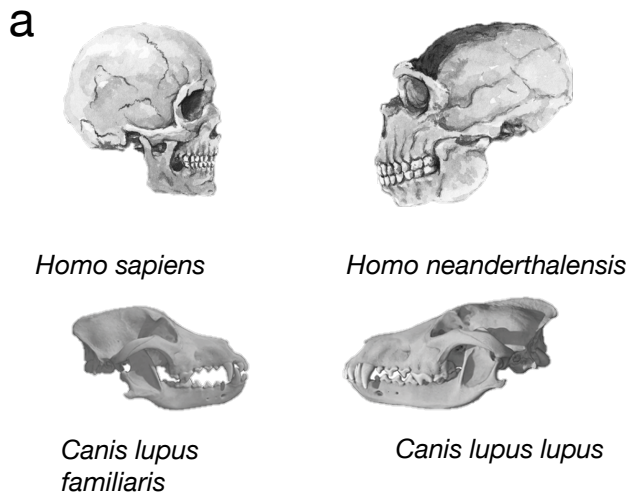
# Gene expression under human self-domestication: an *in silico* exploration of modern human high-frequency variants

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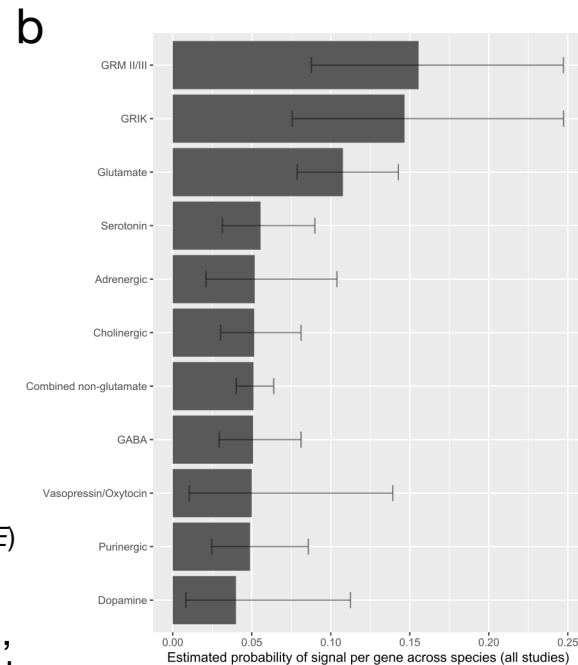


## Convergent human-domesticate evolution

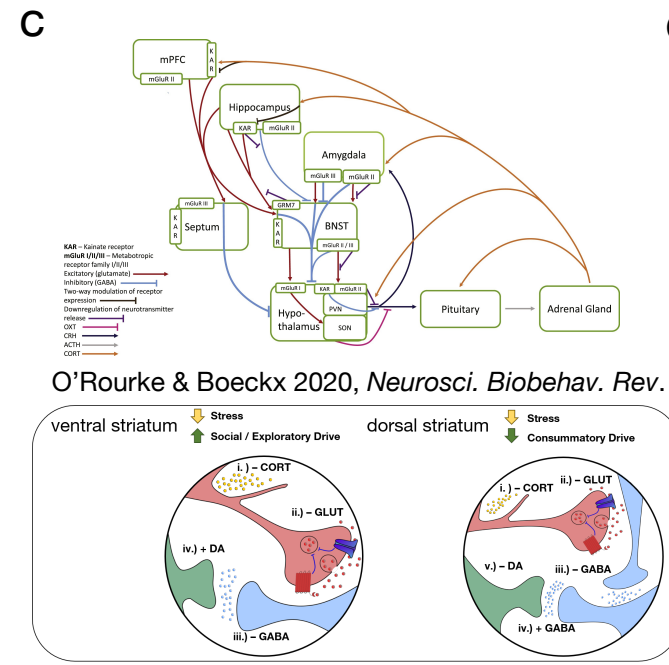


(adapted from Theofanopoulou et al. 2017, *PLoS ONE*)

**Shared Differences:** Craniofacial alterations, attenuated stress signaling, reduced reactive aggression, increased social exploration



O'Rourke & Boeckx 2020 *Neurosci. Biobehav. Rev.*



O'Rourke et al. 2021 *Trends Cogn. Sci.*

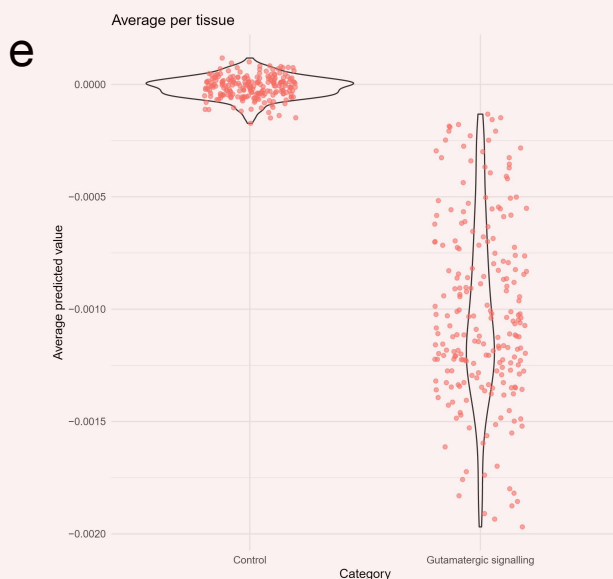
## Hypothesis

- d. Downregulated glutamatergic synaptic activity as a result of positive selection in modern humans

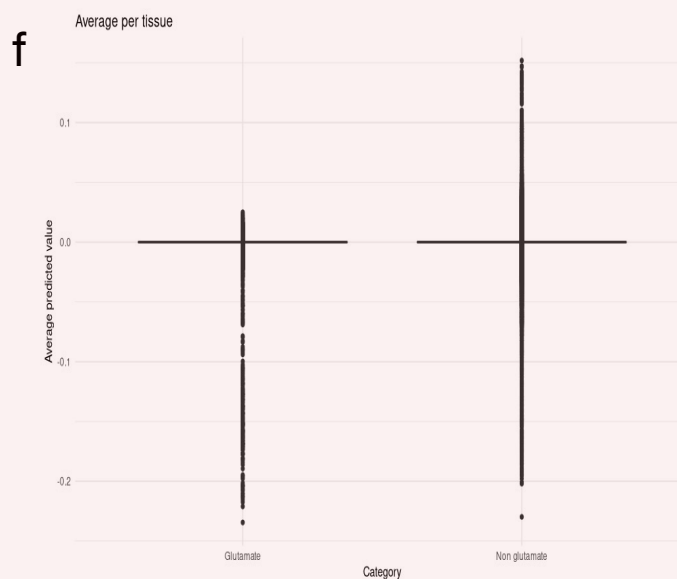
## Methods

- Using [ExPecto](#), we explored predicted expression resulting from high-frequency/fixed variants identified by [Peyrègne et al. 2017](#)
- We generated  $\approx 1$  million predicted transcriptional reads across 218 human tissues
- We compared genes enriched at the Glutamatergic Synapse (GO category [0098978](#)) with other genes targeted in recent human evolution

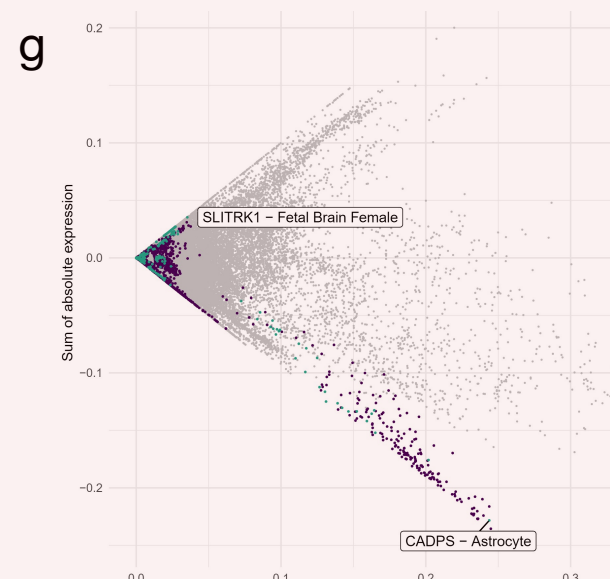
## Results



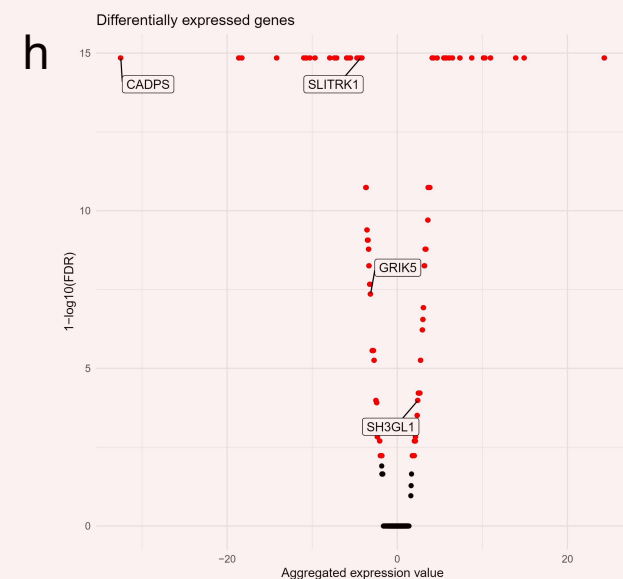
e. Glutamatergic signaling gene variants are significantly downregulated ( $p < 0.01$ ) compared to non-glutamatergic variants when averaged across tissues (red dots)



f. Range of up- and downregulated expression for individual glutamatergic signaling gene versus non-glutamatergic variants. Horizontal lines at zero denote no change in expression



g. Tendency towards downregulation of glutamatergic signaling genes across all tissues (purple) and in brain tissues (blue) versus other genes (grey)



h. Significantly differentially expressed genes (red, FDR < 0.01), including glutamatergic signaling genes (named). Genes left of the zero are downregulated