Human-Specific Modifier of Cortical Circuit Architecture and Circuit Function Improves Behavioral Performance

September 27

Tuesday, 12:30pm

Hybrid: Rosedale Room and Zoom

For Researchers

Speaker:

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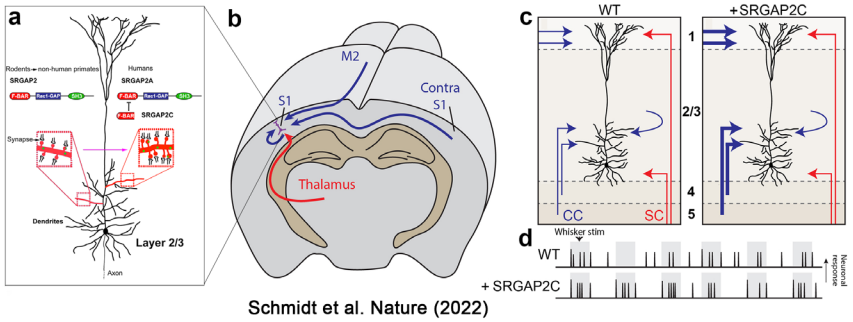
Abstract

The cellular, molecular and genetic mechanisms underlying human brain evolution are still poorly understood. More specifically, the molecular basis underlying human-specific features of synaptic development or synaptic plasticity is largely unknown. Two distinctive features of human cortical circuits are (1) prolonged synaptic development and (2) increased number of excitatory and inhibitory synapse per pyramidal neurons.

Our lab identified a human-specific gene duplication called SRGAP2C which, by inhibiting all known functions of the post-synaptic protein SRGAP2A, leads to slower rates of excitatory (E) and inhibitory (I) synaptic maturation and increased synaptic density (Charrier et al. Cell 2012; Fossatti et al. Neuron 2016). We have recently shown that this increased density of E synapses in cortical layer 2/3 pyramidal neurons (PNs) originates from increased cortico-cortical connections and leads to changes in the coding properties of these neurons in vivo as well as improved behavioral performance in a sensory discrimination task (Schmidt et al. Nature 2021).

These results suggest that the emergence of SRGAP2C at the birth of the Homo lineage, ~ 2.5 million years ago, contributed to the evolution of some of the unique structural and functional features of cortical circuits in the human brain.



Schmidt et al. Nature (2022)

1. Schmidt, E.R.E., Zhao, H.T., Park, J.M., Dipoppa, M., Monsalve-Mercado, M.M., Dahan, J.B., Rodgers, C.C., Lejeune, A., Hillman, E.M.C., Miller, K.D., Bruno, R.M., and Polleux, F. (2021). **A human-specific modifier of cortical connectivity and circuit function.** Nature 599, 640-644.

2. Geiller, T., Sadeh, S., Rolotti, S.V., Blockus, H., Vancura, B., Negrean, A., Murray, A.J., Rozsa, B., Polleux, F., Clopath, C., and Losonczy, A. (2022). **Local circuit amplification of spatial selectivity in the hippocampus.** Nature 601, 105-109.

3. Blockus, H., Rolotti, S.V., Szoboszlay, M., Peze-Heidsieck, E., Ming, T., Schroeder, A., Apostolo, N., Vennekens, K.M., Katsamba, P.S., Bahna, F., Mannepalli, S., Ahlsen, G., Honig, B., Shapiro, L., de Wit, J., Losonczy, A., and Polleux, F. (2021). **Synaptogenic activity of the axon guidance molecule Robo2 underlies hippocampal circuit function.** Cell Rep 37, 109828.

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