Brain circuit rewiring and its consequences in learning and memory

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Meanwhile the adult brain retains a considerable capacity for circuit formation, adult wiring has not been broadly considered and remain poorly understood (Seng et al., 2022). Previously, we identified the transcriptomic regulator Id2 as a key inducer of recurrent mossy fiber sprouting in hippocampal granule cells (Luo et al., 2021). Here, we investigated if the wiring induction by Id2 was generalizable to other adult neurons. We show that Id2 induces axon growth in adult mouse hippocampal CA1 pyramidal cells (PYRs) increasing their connectivity to multiple extrahippocampal areas, including the medial prefrontal and perirhinal cortices (mPFC and Prh), amygdala (Amy), lateral septum (LS) and nucleus accumbens (NAc). In addition to wiring, Id2 increases and restores the excitability of adult PYRs to their young adult level. Finally, we show that Id2 activation in PYRs improves the animals' performance in certain hippocampal-based learning and memory tasks. Together, our results indicate that brain wiring in adults can be reactivated by cell autonomous molecular programing and may be used to enhance cognitive performance.