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HOT TOPICS

New myelin for old memories

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Making and storing memories requires an exquisite balance of plasticity and stability, combining flexible information coding and high-fidelity storage for accurate recall. How new memories are incorporated into existing networks and if/how these networks remain stable over long periods of time remains an active area of investigation.

Emerging evidence suggests that experience-dependent myelination is an important form of plasticity in the adult brain. In rodents, oligodendrogenesis is reduced after social isolation [1] and increased after motor [2] or spatial learning [3]. Our recent work indicates that context fear learning can rapidly induce oligodendrocyte precursor cell (OPC) proliferation and differentiation into myelinating oligodendrocytes (OLs) in the medial prefrontal cortex (mPFC) [4]. Mice lacking the ability to generate new myelin have impaired recall of remote but not recently formed fear memories. In addition, pharmacological interventions that increase new myelin formation strengthen remote fear memory recall in normal mice [4].

These studies raise the intriguing possibility that experience-dependent myelination promotes the coupling of ensembles across brain regions to support the generation of a coordinated fear memory network. After fear learning, OPCs proliferate and mature into myelinating OLs in the mPFC [4], and manipulating myelin formation alters activity and coordination in neural ensembles across the entire hippocampal–prefrontal–amygdala network [3, 4]. Fundamental mechanistic questions about this process remain. For example, while fear learning-induced oligodendrogenesis is rapid, compact myelin takes weeks to form [4]. How experience-dependent OL production may modulate circuit function across these different time scales to support distinct stages of memory is an important area of future investigation. In addition, identifying the cortical axons that become myelinated after fear learning and determining the activity-dependent and/or molecular mechanisms that select axons for myelination can shed important insight into how fear memories are consolidated. Development of tools for regional or cell type-specific manipulations of new myelin formation will enable more targeted experiments. Pairing this with high density, brain-wide recording techniques [5] will provide unprecedented insight into how experience-dependent myelination may serve to organize memory ensembles for temporally precise information flow.

While some memories fade away in a few days, many do not, especially in the case of traumatic memories, which can be recalled with high precision years later. This emerging field identifies a glial-based mechanism for the systems-level consolidation of a fear memory and thus presents a novel potential target for the treatment of memory-related anxiety disorders, such as post-traumatic stress disorder (PTSD). Increased hippocampal myelin content has been documented in combat veterans with PTSD [6], implicating aberrant myelination in the pathophysiology of an anxiety disorder. In mouse models, compact myelin formation takes place over several weeks after a fearful experience, and pharmacologically increasing new myelin over this time window can both promote long-term fear memory recall and fear memory generalization [4]. Thus, it may be that an optimal set point for experience-induced myelination is required for maintaining precise remote memory recall while reducing overgeneralization. By targeting new myelin in the adult brain, we may more precisely and less invasively modulate neuronal function to shape emotional memories and alleviate anxiety-related behavior.

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M.A.K. and M.C.K. wrote the manuscript.

ADDITIONAL INFORMATION

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