Impact of age-related perturbations on a bump attractor model of working memory

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Normal aging in humans and non-human primates is associated with progressive cognitive changes, which are especially evident in working memory tasks. Working memory is governed by the dorsolateral prefrontal cortex (dlPFC), that is undergoing pronounced alterations during normal aging, including myelin loss, synapse loss, and neuronal hyperexcitability. Despite a wealth of experimental data, a coherent theoretical framework of how these age-related neuronal changes interact and alter network dynamics in normal aging is currently lacking. Here, we investigated how both the individual and shared contributions of aging factors can lead to working memory decline in bump attractor networks.

We developed a bump attractor network that models the dynamics of the dlPFC neural representations underlying spatial working memory, incorporating two key aging factors: myelination deficits and neuronal hyperexcitability. The simulations were carried out using an adaptation of a spiking neural network consisting of excitatory and inhibitory populations of leaky integrate-and-fire neurons with sparse connectivity, that also incorporate short-term synaptic depression and facilitation (Hansel and Mato, 2013). Demyelination was modeled as an increase in the action potential failure rate (Ibañez et al., 2023), and changes in excitability were introduced by modifications to the f-I curve of leaky integrate-and-fire neurons, fitted to empirical data (Ibañez et al., 2020).

Our models predict that biologically plausible levels of myelin loss and hyperexcitability can account for substantial working memory impairment with aging, although via distinct mechanisms. Hyperexcitability leads to a spread of activity among neurons and increased

neuronal correlations within the network. Consistent with theory, these changes in the network dynamics lead to increased diffusion of the activity bump and therefore predict less precise working memory representations.
In contrast, myelin loss severely impacts the amplitude but not the width of the activity bump, resulting in reduced firing rate levels and stability over time, thereby primarily impairing memory duration.
These findings highlight the different impacts of age-related changes on working memory circuit functionality, providing insights into the mechanisms of cognitive decline along with potential pathways for prevention and treatment.

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