Working memory (WM) emerges from distributed neural activity across cortical areas sustained by inter-areal reverberation. Large-scale models of macaque cortex have shown that persistent activity can arise even when individual regions cannot maintain it in isolation, giving rise to distributed attractor states along the cortical hierarchy (Mejías et al., 2021). Here, we capitalize on these findings and study how working memory function is altered by structural changes occurring during normal aging.

Aging is associated with synaptic alterations, including reduced dendritic spine density and changes in both local and long-range connectivity, which are likely to disrupt these dynamics. To investigate this, we extend a biologically constrained large-scale cortical model (Mejías et al., 2021), and, as a first step, incorporate age-dependent reductions in synaptic efficacy to mimic loss of excitatory synapses. We find that this gradually reduces the stability of attractor states. Networks with reduced synaptic efficacy also become more vulnerable to perturbations: inactivation of only a few areas is sufficient to loose sustained activity. Notably, localized working memory (LWM) networks, where individual cortical areas locally sustain reverberation, are less robust, whereas distributed working memory (DWM) networks, where persistent activity relies more on inter-area reverberation, sustain persistent activity. However, in both LWM and DWM networks, robustness to distractors was lost when decreasing synaptic strengths.

Together, these results suggest that aging selectively weakens the stability and robustness of distributed cortical attractor states, providing a potential mechanistic explanation for increased distractibility and working memory deficits observed in aging.