Post-Translational Regulation of AMPA Receptors: A Key to Aging-Associated Cognitive Decline

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Memory decline is a hallmark of aging, yet the underlying molecular mechanisms remain largely elusive. Previous studies have established that AMPA receptors (AMPARs) play a pivotal role in memory acquisition and storage. Based on these findings, we hypothesize that in the aging brain, AMPARs undergo aging-specific post-translational modifications (AMPAR-PTMs), which compromise their ability to support memory storage. To test this hypothesis, we first delineated the subunit-specific dynamics of AMPARs in young brains, elucidating their distinct roles in memory acquisition and retention. In this study, we first aim to clarify the detailed dynamics of AMPA receptor subunits in the brain before aging (young brain), and then to perform proteomic analysis of AMPA receptor subunits in the aging brain, with the aim of identifying AMPAR-PTM that occurs specifically in the aging brain and proving this hypothesis. In this study, we clarified the role of AMPA receptor subunits in the acquisition and maintenance of memory function in the young brain. These insights lay the groundwork for uncovering the molecular basis of age-related memory decline and identifying potential therapeutic targets.