Defining the genetic basis for individual differences in learning, 2013 - 2015

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Genome-wide screening studies have suggested a strong association between a single nucleotide polymorphism in the *KIBRA* gene and human memory performance. This gene encodes an intracellular protein Kibra that is expressed in mouse brain and cultured neurons. A recent study from Huganir and colleagues found that Kibra is a key molecule that modulates the synaptic trafficking of AMPA receptors, the major excitatory neurotransmitter receptors in the brain, and also regulates synaptic plasticity and learning and memory in mice. The proposed research attempts to use cognitive and imaging approaches to further investigate the genetic association of *KIBRA* variants with human memory, and then explore the molecular and cellular mechanisms underlying Kibra’s effect on memory in mouse model systems. It will expand the current genetic-behavior association studies in humans by combining them with rigorous molecular, cellular, physiological and behavioral studies of the function of identified *KIBRA* SNPs on AMPA receptor trafficking in neuronal cell cultures, and synaptic plasticity and learning and in Kibra mutant mouse. These studies will define the molecular basis underlying the individual differences in human memory performance caused by *KIBRA* genetic variants and identify new pathways in the regulation of learning and memory and may provide novel therapeutic targets for the treatment of human memory disorders.

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