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GENOME-WIDE SEARCH FOR GENES ASSOCIATED WITH MEMORY-RELATED BRAIN ACTIVATION PATTERNS

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Background: Human memory is a polygenic trait. Heritability estimates of ~50% suggest that genetic factors have an important impact on this fundamental brain function.

Objectives:

1. To identify genes and gene-clusters related to memory capacity and to brain activation during memory tasks;
2. To translate the findings to memory-related disorders.

Methods: A combination of genome-wide association studies (GWAS), candidate gene studies (gene clustering) and functional MRI (fMRI) in independent populations which were carefully tested for episodic memory performance and for the presence or absence of Alzheimer's disease.

Conclusions: Variability of human memory performance is related to variability in genes encoding proteins of important signaling cascades, including NMDA receptor, metabotropic glutamate receptor, adenylyl cyclase, CAMKII, PKA and PKC. Functional magnetic resonance imaging reveals that this genetic profile correlates with activations in memory-related brain regions. GWAS reveal the existence of novel genes significantly related to human memory performance, brain activation and to the risk for developing Alzheimer's disease.