Functional analysis of human genetic variant in BDNF (Val66Met)

Summary
A common single nucleotide polymorphism (SNP) in the brain-derived neurotrophic factor gene (Val66Met) is associated with alterations in brain anatomy and memory, but its relevance to clinical disorders is unclear. We have generated a transgenic variant BDNF mouse (BDNFMet/Met) that reproduces the phenotypic hallmarks in humans with the variant allele. In this mouse, variant BDNFMet expression in brain is normal, but its secretion from neurons is defective. When placed in stressful settings, BDNFMet/Met mice also exhibit increased anxiety-related behaviors that are not normalized by the antidepressant, fluoxetine. These findings indicate that an allelic variant BDNF may play a role in the genetic predisposition in humans to anxiety and depressive disorders.