
Abstract:
The Val(108/158)Met polymorphism of the catechol-O-methyltransferase gene (COMT) is known to interact with the function of various neuroreceptor systems in the brain. We have recently shown by post-mortem receptor autoradiography that the number of mu-opioid (MOP) receptor binding sites depends on the number of COMT Met(108/158) alleles in distinct human brain regions. We now investigated COMT Val(108/158)Met related levels of the MOP receptor protein and its endogenous ligands met-enkephalin and beta-endorphin in the human frontal cortex, thalamus and basal ganglia. Semiquantitative immunostaining and in situ hybridization were applied in a cohort of 17 human brain tissues from healthy donors. MOP receptor protein levels paralleled previous ligand binding results with a significantly higher MOP receptor expression in the mediodorsal nucleus of the thalamus of COMT Met(108/158) allele carriers. Also met-enkephalin peptide levels correlated with the genotype in this structure, with the lowest expression in COMT Met(108/158) homozygous individuals. Beta-endorphin was not detectable in the cortex, basal ganglia or thalamus, and therefore is unlikely to contribute to changes of the MOP receptor system. These results confirm the impact of the COMT Val(108/158)Met polymorphism on the
MOP receptor system and may support the hypothesis of an enkephalin related turnover of MOP receptors at least in some brain structures.

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