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Distribution of Cytochrome P450 2D6 in the human brain: potential role in psychotropic drug response

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Background

The cytochromes P450 (CYP450) 1-3 are involved in 70-80% of all phase-I dependent metabolism of drugs. Highly polymorphic CYP450 2D6 gene is coding biotransformation of about 25% of clinically used medications, including opioid analgesics, antipsychotics and antidepressants. Its liver tissue expression is well investigated, but still controversial information is available regarding the presence in the human brain, as well as the contribution to psychotropic drug actions and adverse drug reactions. This review followed-up the published data according to the localization, regional distribution and protein expression of CYP 2D6 in CNS and analyzed the current information about its role in local drug pharmacokinetics and drug response.

Materials and methods

MEDLINEplus, PubMed, Entrez and Medscape databases and electronic journals were searched for studies on CYP 2D6 in the human brain. Published research articles and reviews on pharmacogenetics of oxidative metabolism and psychotropic drug response were observed for the potential role of CYP 2D6 brain expression.

Results

Reviewed studies demonstrated CYP2D6 distribution, CYP2D6 mRNA and protein constitutive expression in neuronal and glial cells in certain CNS regions [1-3]. Some data supported differences in brain CYP2 induction, depending on the region, cell type and inducer. CYP2D6 was found to be involved in the brain endogenous substances metabolism and its enzyme activity could be under various regulatory mechanisms with potential influence on drug response [4].

Conclusions

Constitutive expression of CYP2D6 in CNS may create a local environment of drug metabolism, which, along with the potential neurotransmitter modulation, may contribute to altered sensitivity and inter-individual variability in psychotropic drug response.

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