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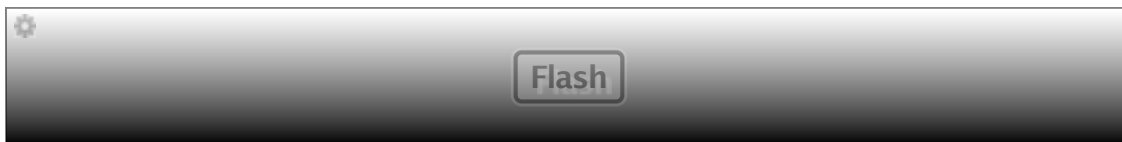
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CYP2D6 in the brain: genotype effects on resting brain perfusion.

Kirchheiner J, Seeringer A, Godoy AL, Ohmle B, Maier C, Beschoner P, Sim EJ, Viviani R
Mol Psychiatry. 2011 Mar; 16(3):237, 333-41

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PubMed Abstract

Magnus Ingelman-Sundberg, Karolinska Institutet, Sweden. **F1000**
Pharmacology & Drug Discovery

08 Mar 2011 | Novel Drug Target

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This is the first study to show a plausible role of cytochrome P4502D6 (CYP2D6) in the human brain. This is of sincere interest due to the previously described link between CYP2D6 polymorphism and personality and, more recently, to studies concerning the increased risk for suicide among ultrarapid metabolisers (UM) of CYP2D6.

In 1993, the first example of a stable gene duplication and gene amplification in the human genome was identified causing the UM phenotype, where subjects carrying > 2 active gene copies of the CYP2D6 gene {1}, were found to have very high capacity for the metabolism of, for example, tricyclic antidepressants. Such subjects have been shown to be overrepresented among non-responders of antidepressant therapy and were also found by Zachrisson et al. {2}, to be overrepresented among suicides. Furthermore, Peñas-Lledó et al. {3} found a higher suicide risk among UMs of CYP2D6 and a similar relationship was also described independently by Stingl and Viviani {4}. Julia Stingl (formerly Kirchheiner) and collaborators describe here the association between the presence of CYP2D6 in the brain, and decreased perfusion levels in the thalamus and, to some extent, in the hippocampus, suggesting the involvement of CYP2D6 in regions associated with alertness or serotonergic function. This is of severe interest in order to possibly identify a physiological function of CYP2D6 and to provide a possible molecular explanation for an association between CYP2D6 polymorphism, personality, and suicide risk.

NB: Magnus Ingelman-Sundberg is an author on ref {1}.

References:

- {1} Johansson et al. Proc Natl Acad Sci USA 1993, 90:11825-9 [PMID:7903454].
- {2} Zachrisson et al. Clin Pharmacol Ther 2010, 88:354-9 [PMID:19907421].
- {3} Peñas-Lledó et al. Mol Psychiatry 2011, Feb 15, Epub ahead of print [PMID:21321564].
- {4} Stingl and Viviani, Clin Pharm Ther 2011, 89:352-3 [PMID:21248727].

Competing interests: None declared

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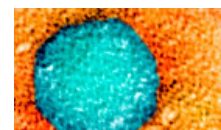
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