

## Original Article

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

J Kirchheiner<sup>1</sup>, A Seeringer<sup>1</sup>, A L Godoy<sup>1,5</sup>, B Ohmle<sup>1</sup>, C Maier<sup>2</sup>, P Beschoner<sup>3,4</sup>, E-J Sim<sup>3</sup> and R Viviani<sup>3</sup>

<sup>1</sup>Institute of Pharmacology of Natural Products and Clinical Pharmacology, University of Ulm, Ulm, Germany

<sup>2</sup>Institute of Human Genetics, University of Ulm, Ulm, Germany

<sup>3</sup>Department of Psychiatry and Psychotherapy III, University of Ulm, Ulm, Germany

<sup>4</sup>Department of Psychosomatic Medicine and Psychotherapy, University of Ulm, Ulm, Germany

<sup>5</sup>Faculty of Pharmaceutical Sciences de Ribeirão Preto, University Ribeirão Preto, Brazil

Correspondence: Dr J Kirchheiner, University of Ulm, Institute of Pharmacology of Natural Products and Clinical Pharmacology, Helmholtzstr 20, Ulm D-89081, Germany. E-mail: [julia.kirchheiner@uni-ulm.de](mailto:julia.kirchheiner@uni-ulm.de)

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## Abstract

**The cytochrome P450 2D6 (CYP2D6) is a genetically polymorphic enzyme involved in the metabolism of several psychoactive drugs. Beside its expression in the liver, CYP2D6 is highly expressed in several regions of the brain, such as the hippocampus, thalamus, hypothalamus and the cortex, but its function in the brain is not well understood. The CYP2D6 enzyme may also have a physiological role due to its involvement in neurotransmitter biotransformation. In this study, CYP2D6 genotyping was performed in  $N=188$  healthy individuals and compared with brain perfusion levels at rest, which may reflect an ongoing biological process regulating the reactivity of the individual to emotional stimuli and the detection of signals evoking fear. Relative to  $N=42$  matched extensive metabolizers,  $N=14$  poor metabolizers were associated with 15% higher perfusion levels in the thalamus ( $P=0.03$  and  $0.003$ ). Effects were also present in the whole ( $N=188$ ) sample divided into metabolizer groups, or finely graded into seven CYP2D6 activity levels. A weaker effect was observed in the right hippocampus ( $P=0.05$ ). An exploratory analysis, extended to the whole brain, suggested the involvement of CYP2D6 in regions associated with alertness or serotonergic function. These findings support the hypothesis of a functional role of CYP2D6 in the brain.**

**Keywords:** CYP2D6; resting brain perfusion; arterial spin labeling

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