Effect of antidepressants on cytochrome P450 (CYP) 2D6-mediated dopamine formation from \( p \)-tyramine

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**[Purpose]** CYP2D catalyze dopamine formation from \( p \) and \( m \)-tyramine in the brain, and human CYP2D6 is polymorphic. Imipramine, a tricyclic antidepressant, and fluvoxamine, an SSRI, are CYP2D6 inhibitors. Dopamine formation from \( p \)-tyramine mediated by CYP2D6 variants, CYP2D6.2 and CYP2D6.10 was compared, and the effect of genetic polymorphism on the inhibitory effects of antidepressants was investigated.

**[Methods]** CYP2D6.1, CYP2D6.2, and CYP2D6.10 expressed in recombinant *Escherichia coli* were used. Dopamine formation from \( p \)-tyramine in the presence of antidepressants such as imipramine, desipramine, fluvoxamine, fluoxetine, and paroxetine was determined by HPLC.

**[Results]** CYP2D6.10 had higher Michaelis constants of dopamine formation than CYP2D6.1 and CYP2D6.2. Inhibition constant of imipramine and desipramine against CYP2D6.10 were higher than that against CYP2D6.1. Fluoxetine and paroxetine inhibited CYP2D6.1-mediated dopamine formation. The maximal velocity for all CYP2D6 variants gradually increased with increasing fluvoxamine concentrations.

**[Conclusions]** CYP2D6 polymorphism might affect the inhibitory effect of antidepressants on dopamine formation in the brain.