Fluoxetine

Class: Antidepressants, Selective Serotonin Reuptake Inhibitor (SSRI)

Pharmacokinetics

Absorption

i.) Non-genetic
   a. Food: decreases absorption rate but not extent

ii.) Genetic
   a. No clear genetic factors affecting absorption

Distribution

i.) Non-genetic
   a. Altered serum protein (94.5% protein bound to albumin and alpha-1 acid glycoprotein)
   b. Concomitant medications: highly protein-bound drugs may displace fluoxetine from protein binding sites; fluoxetine may displace other drugs from protein binding sites

ii.) Genetic
   a. No clear genetic factors affecting absorption

Metabolism

i.) Non-genetic
   a. Concomitant medications/substances: CYP2C9, **CYP2D6** inducers or inhibitors
   b. Hepatic impairment: decreased metabolism (prolonged elimination half-life)

ii.) Genetic
   a. Genetic variation in drug metabolizing enzyme gene(s): CYP2C9, **CYP2D6**

Excretion

i.) Non-genetic
   a. No clear non-genetic factors affecting excretion

ii.) Genetic
   a. No clear genetic factors affecting excretion

Pharmacodynamics

Receptors

i.) Non-genetic
   a. Concomitant medications/substances: serotonin receptor agonists or antagonists (may block or enhance effects of fluoxetine)

ii.) Genetic
   a. Genetic variation in serotonin receptor gene(s)
   b. Genetic variation in G-protein beta-3 subunit gene
   c. Genetic variation in Gs protein alpha-subunit gene

Transporters

i.) Non-genetic
   a. Concomitant medications/substances: serotonin transporter inhibitors (additive effects)

ii.) Genetic
   a. Genetic variation in serotonin transporter gene