

Symposium | Psychopharmacology : [Symposium 49] Cultural Psychopharmacology: Integrating Genetics, Ethnicity, and Global Perspectives

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## [Symposium 49] Cultural Psychopharmacology: Integrating Genetics, Ethnicity, and Global Perspectives

Moderator: Kazutaka Shimoda (Tochigi Prefectural Okamoto Hospital)

### [SY-49-01] CYP2D6 Genotype, BMI, and Culture: Rethinking Antipsychotic Dosing Across the U.S., China, and Japan

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Keywords : Pharmacogenomics、CYP2D6 polymorphism、Antipsychotic dosing、Cultural psychiatry、Precision medicine

#### Background:

Antipsychotic dosing typically targets about 78% D2 receptor occupancy to balance effectiveness with side effects. However, average prescribed doses vary widely between countries, making explanations based solely on pharmacokinetics difficult.

#### Objective:

To investigate how CYP2D6 genotypes, BMI, and cultural prescribing practices together affect antipsychotic dosing in the United States, China, and Japan.

#### Methods:

Published CYP2D6 metabolizer distributions (Gaedigk et al., CPIC 2017) were combined with average BMI data (WHO Global Database) to estimate the chlorpromazine (CPZ)-equivalent doses required to achieve target D2 occupancy. Calculations included adjustments for enzyme activity and BMI-based volume of distribution models. Actual national averages were derived from large-scale studies involving over 15,000 patients combined (Leucht et al., 2014; Zhang et al., 2013; Inada et al., 2015).

#### Results:

Predicted mean CPZ equivalents were 400 mg (U.S.), 252 mg (China), and 268 mg (Japan). However, actual averages were significantly higher: 400 mg (U.S.), 452 mg (China, +200 mg vs. predicted), and 675 mg (Japan, +407 mg). Biological factors (CYP2D6 + BMI) explained about 38% of the total dose variation (variance estimate based on comparative multi-factor models), with the remainder shaped by systemic, institutional, and cultural factors.

#### Conclusion:

Antipsychotic dosing cannot be determined solely by pharmacokinetics. Japan's emphasis on long-term hospitalization and physician autonomy, China's rapid stabilization pressures in urban outpatient settings, and the U.S.'s cautious, litigation-sensitive approach show how local treatment philosophies and healthcare systems take precedence over biological expectations. Implications:

These findings highlight the need for developing culturally sensitive and contextually appropriate pharmacogenomic guidelines. Precision psychiatry should go beyond receptor occupancy by integrating systems thinking and local values. Including non-D2 mechanisms and digital phenotyping may further enhance culturally sensitive, patient-centered models of global mental health care.