How coffee and cigarettes can affect the response to psychopharmacotherapy

When a patient who smokes enters a tobacco-free medical facility and has access to caffeinated beverages, he (she) might experience toxicity to many pharmaceuticals and caffeine. Similarly, if a patient is discharged from a smoke-free environment with a newly adjusted medication regimen and resumes smoking or caffeine consumption, alterations in enzyme activity might reduce therapeutic efficacy of prescribed medicines. These effects are a result of alterations in the hepatic cytochrome P450 (CYP) enzyme system.

Taking a careful history of tobacco and caffeine use, and knowing the effects that these substances will have on specific medications, will help guide treatment and management decisions.

The role of CYP enzymes
CYP hepatic enzymes detoxify a variety of environmental agents into water-soluble compounds that are excreted in urine. CYP1A2 metabolizes 20% of drugs handled by the CYP system and comprises 13% of all the CYP enzymes expressed in the liver. The wide interindividual variation in CYP1A2 enzyme activity is influenced by a combination of genetic, epigenetic, ethnic, and environmental variables.1

Influence of tobacco on CYP
The polycyclic aromatic hydrocarbons in tobacco smoke induce CYP1A2 and CYP2B6 hepatic enzymes.2 Smokers exhibit increased activity of these enzymes, which results in faster clearance of many drugs, lower concentrations in blood, and diminished clinical response. The Table (page 80) lists psychotropic medicines that are metabolized by CYP1A2 and CYP2B6. Co-administration of these substrates could decrease the elimination rate of other drugs also metabolized by CYP1A2. Nicotine in tobacco or in nicotine replacement therapies does not play a role in inducing CYP enzymes.

Psychiatric patients smoke at a higher rate than the general population.2 One study found that approximately 70% of patients with schizophrenia and as many as 45% of those with bipolar disorder smoke enough cigarettes (7 to 20 a day) to induce CYP1A2 and CYP2B6 activity.2 Patients who smoke and are given clozapine, haloperidol, or olanzapine show a lower serum concentration than non-smokers; in fact, the clozapine level can be reduced as much as 2.4-fold.2,5 Subsequently, patients can experience diminished clinical response to these 3 psychotropics.3

The turnover time for CYP1A2 is rapid—approximately 3 days—and a new CYP1A2 steady state activity is reached after approximately 1 week,4 which is important to remember when managing inpatients in a smoke-free facility. During acute hospitalization, patients could experience drug toxicity if the outpatient dosage is maintained.3
When they resume smoking after being discharged on a stabilized dosage of any of the medications listed in the Table, previous enzyme activity rebounds and might reduce the drug level, potentially leading to inadequate clinical response.

### Caffeine and other substances

Asking about the patient’s caffeine intake is necessary because consumption of coffee is prevalent among smokers, and caffeine is metabolized by CYP1A2. Smokers need to consume as much as 4 times the amount of caffeine as non-smokers to achieve a similar caffeine serum concentration. Caffeine can form an insoluble precipitate with antipsychotic medication in the gut, which decreases absorption. The interaction between smoking-related induction of CYP1A2 enzymes and forced smoking cessation during hospitalization, with ongoing caffeine consumption, could lead to caffeine toxicity.4,5

Other common inducers of CYP1A2 are insulin, cabbage, cauliflower, broccoli, and charcoal-grilled meat. Also, cumin and turmeric inhibit CYP1A2 activity, which might explain an ethnic difference in drug tolerance across population groups. Additionally, certain genetic polymorphisms, in specific ethnic distributions, alter the potential for tobacco smoke to induce CYP1A2.6

Some of these polymorphisms can be genotyped for clinical application.3

Asking about a patient’s tobacco and caffeine use and understanding their interactions with specific medications provides guidance when prescribing antipsychotic medications and adjusting dosage for inpatients and during clinical follow-up care.

### References