Comorbid Conditions Need Integrated Treatment

BY KATE JOHNSON Montreal Bureau

MONTREAL — Comorbid eating disorders and substance abuse are intertwined behaviorally and biologically, so the treatment of both problems must be an integrated effort, Cynthia M. Bulik, Ph.D., said at an international conference sponsored by the Academy for Eating Disorders.

And with growing numbers of middle-aged women presenting to eating disorder programs, substance abuse comorbidity is being seen more frequently than in the teenage population, she said.

We don't have sufficient integrated treatment programs, so often patients will go to substance abuse programs, which either ignore or are ill equipped to deal with their eating disorder, and then they are sent to an eating disorders program without necessarily the proper followup for their substance abuse," said Dr. Bulik, professor of eating disorders and nutrition at the University of North Carolina, Chapel Hill.

Although the abuse of substances, such as laxatives or diet pills, may have superficial connections to the desire for weight loss, the abuse is almost always intertwined with other complex psychiatric issues, noted Dr. Bulik.

"If we try to discourage a patient from abusing laxatives by pointing out that they are ineffective as weight loss agents, we are missing the mark clinically, because there's a real self-harm component to this behavior," she said in an interview. "When a person takes 50 laxatives a day, it hurts, there's incredible cramping and diarrhea, it keeps them up at night, and it's very painful. If we fail to address this whole self-punishing aspect, we're really not addressing their needs.

Indeed, she and her associates have found that laxative

abuse, most common among patients with purging anorexia (72%) and combined anorexia and bulimia nervosa (59%), is associated with a significantly higher prevalence of borderline personality disorder—characterized particularly by feelings of suicidality, self-harm, emptiness, and anger, she reported.

In another study, Dr. Bulik and her associates found that alcohol abuse is more prevalent in patients with bulimia (46%) and combined bulimia and anorexia (37%), compared with those with anorexia (16%) alone (J. Clin. Psychiatry 2004;65:1000-6). Other studies have suggested anywhere from two to six times the risk of alcohol dependency in the eating disordered population, compared with the general population, she said.

As with laxative abuse, alcohol abuse in patients with eating dis-

these drugs can actually be part of the eating disorder.

Research suggests that smoking can significantly increase resting energy expenditure, making it counterproductive to treatment because it can interfere with the treatment goal of weight restoration; caffeine is used to overcome some of the fatigue caused by undernourishment. "There's both a cognitive component and a physiologic component to this kind of drug use. Patients know that nicotine increases their metabolism, and they know that caffeine might be giving them false energy when they are not eat-

ing," she said. In addition, cravings for all drugs are enhanced with food deprivation, a neurobiologic factor that could interfere with drug abuse rehabilitation.

"People need reinforcers, and food is the major reinforcer. Just like in laboratory animals, when you take food away, they often turn to other substances," Dr. Bulik said.

Careful attention to patterns and changes in patients' substance abuse can offer important insight when tracking their eating disorder, and vice versa. It can also help in the prediction or prevention of relapse.

As an example, she described a person who may have gained control of her eating disorder but not her alcohol abuse. Because alcohol disinhibits appetite, it could trigger binge eating that could trigger a relapse of the eat-

Similarly, if a patient is unable to decrease her nicotine consumption, this could be an indication that her eating disorder is not well controlled.

We need to focus on integrated treatments where we are dealing with both things at the same time, looking at how they interrelate, understanding what some of the overarching integrators might be, and exploring how substances can influence relapse," Dr. Bulik said.

orders occurs with other psychiatric comorbidities such as major depressive disorder, obsessive compulsive disorder, posttraumatic stress disorder, social phobia, borderline personality disorder, and perfectionism-all of which need to be evaluated and treated. Dr. Bulik said. ing disorder. Also, other drugs such as nicotine and caffeine should be considered more problematic in patients with eating disorders than in healthy individuals, she said. In such patients,

Genetic Tests Could Improve Future Drug Abuse Treatment

BY ERIK L. GOLDMAN Contributing Writer

NEW YORK — Simple genetic tests aimed at predicting the risk of drug addiction are still a long way off. But the genomics revolution is slowly changing the way physicians look at their patients and the disorders they treat.

Wade Berrettini, M.D., of the University of Pennsylvania, Philadelphia, said investigators have identified several single nucleotide polymorphisms (SNPs), small but meaningful allelic variants that result in changes to the shape or structure of a specific receptor or enzyme that relate directly to addiction problems.

Among these is a set of SNPs that influence the binding affinity of the mu β -endorphin receptors. Some of the SNPs in this set are proving to have some predictive value for alcohol and nicotine addiction, and for response to addiction treatment.

The Human Genome Project is really only the beginning," Dr. Berrettini said at annual conference of the Association for Research in Nervous and Mental Disease. "At this point, it is like knowing the alphabet, without knowing words.

Dr. Berrettini's lab has been focused on SNPs in the gene that codes for the mu receptor protein, which plays a central role in generating the neurophysiologically rewarding and analgesic effects of morphine.

Endorphins and enkephalins also bind to the mu receptor. Given its place in mediating the brain's response to endogenous as well as exogenous opioids, the mu receptor also plays an important role in the process of addiction to opioids, as well as other substances, such as alcohol and nicotine.

To date, researchers have identified at least 25 SNP variants in the gene coding

for the mu receptor. It is important to understand that none of these SNPs constitutes a "gene" for addiction, he said. However, some of them do seem to alter how the mu receptor functions. One such SNP, for example, tends to increase the receptor's binding affinity for βendorphin.

Dr. Berrettini and his colleagues have been studying mu receptor SNPs in the

context of heroin addiction. Though they have not yet identified any single variant that clearly shows an increased prevalence among addicts, compared with nonaddicts, they have found some interesting racial differences.

"In African Americans, we've found some alleles in 10% of the population that we simply have not found in people of European ancestry," he said at the conference, cosponsored by the New York Academy of Medicine.

This underscores an important guiding principle for genomic research: When looking at the influence of small genetic variations on the risk of a given disease state, it is important to compare ill versus well people of the same racial and ethnic background.

Prevalence of Alcohol Use

Disorders in Patients

With Eating Disorder

46%

37%

Rulimia

nervosa

Combined

Anorexia

Though Dr. Berrettini's team was unable

to identify a specific mu receptor SNP that correlated with heroin addiction, Swedish researchers were able to do so. They found a variant called A118G that does seem to predict risk of heroin dependence. Approximately 18% of Swedish opioid addicts had disease that is caused in part

by this SNP. Some researchers have suggested that

the mu receptor may play a role in alcohol dependence since ethanol triggers a release of β -endorphin, the key ligand for the mu receptor.

Available data correlating SNPs in the mu receptor gene and alcoholism are highly variable; there are as yet no studies showing a clear association. However, variants in this gene may predict an alcoholic's response to treatment with naltrexone.

Dr. Berrettini and his group have done a series of studies looking at multiple mu receptor SNPs in alcohol-dependent individuals treated with naltrexone. In the subgroup of patients who had either the A/G or G/G variants of the Asp40 allele, only 10% relapsed after nearly 3 months of posttreatment follow-up. Those with the A/A variant had very high relapse rates, and outcomes were no better for naltrexone than placebo. What these data suggest is that response

to this drug, which is a mu receptor blocker, may be largely determined by genetic variants in a specific receptor. Dr. Berrettini estimated that 25% of the alcoholic population is either homozygous or heterozygous for the G allele, and it predicts better response to naltrexone.

Those who are homozygous for the A allele do poorly on this drug. "We'd like to do a treatment study where we randomize based on mu allele genotype," Dr. Berrettini said.

Though still in its early stages, this type of research is opening up the possibility of designing treatment protocols based on an individual's genetic predispositions and likelihood of responsiveness to specific medications. In other words, individualized therapy based on pharmacogenomics may soon become the standard of care.

The technology to screen for SNPs is very well developed, and the cost is rapidly decreasing. "It is definitely possible to do SNP testing in a community hospital setting, and insurance will even pay for some of this," said Dr. Berrettini. "The biggest challenge right now is to make clinical sense of the massive amount of new information we have about the human genome.'



Dr. Wade Berrettini has been studying genetic variants in heroin addicts.