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# Gender Differences Should Be Considered in Treatment of Addiction

Lois Wingerson

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The molecular events that accompany drug abuse and addiction are different for women than for men, according to new studies presented at the annual meeting of the American Psychiatric Association (APA). As yet, little if any of this knowledge has made its way into gender-based differences in pharmacological and behavioral treatments for addiction. But according to some of the speakers, it could and it should.

"It is dangerous at best, and completely wrong at worst, to assume that any neurological disorder has the same underlying causes in men and women, and thus to assume that treatments for the disorder will be essentially the same," said Larry Cahill, PhD, associate professor of neurobiology and behavior at the School of Biological Sciences, University of California, Irvine. "Yet that is precisely the assumption that continues to pervade much of both the clinically applied and basic science worlds."

Even in its epidemiology, addiction shows a gender difference, remarked Jill Becker, PhD, professor of psychology at the University of Michigan, Ann Arbor. Women begin using drugs of abuse at lower doses than men, she said. Their drug use escalates more rapidly to addiction, and they face a greater risk of relapse after abstinence. Laboratory animals show the same kind of gender differences in addiction, which has made it possible to study these phenomena among rats and mice. But there's now plenty of direct evidence from humans.

Women tend to enter treatment sooner after becoming substance dependent than men, but they present with more psychological distress, and particularly with more mood and anxiety disorders, according to research by Christine E. Grella, PhD, research psychologist at the University of California, Los Angeles.<sup>1</sup> Most research on gender-based differences in addiction treatment has focused on organizational issues (such as the greater need to provide women with child care and employment training) rather than on pharmacology. But even this focus does not always make its way into changes in the treatment that is actually provided.

As to differences in gender and pharmacology, studies have focused almost exclusively on dosage and on issues involving pregnancy. The new research presented at the APA meeting offers ample evidence to support a search for new medications that are specifically designed for women with addiction problems.

Addiction is widely viewed as a disorder of memory processes. Over the past several years, studies led by Cahill have shown strong hemispheric gender differences in how the brain

responds in memory processing after seeing emotionally arousing material. For example, men's responses are stronger from the right amygdala, and women show stronger signals from the left amygdala. More recent work has shown noticeable differences of this kind even in the resting condition.<sup>2</sup> Cahill said this research may help to explain previous evidence for effects of the menstrual cycle on craving and also gender differences in the effectiveness of treatments such as the nicotine patch.

There's also direct evidence for effects of the menstrual cycle on phenomena relevant to substance abuse.<sup>3</sup> Using positron emission tomography and functional MRI (fMRI) studies, Karen Faith Berman, MD, and colleagues at the NIMH in Bethesda, Md, have found that fluctuations in steroid hormone levels during the menstrual cycle affect neural responses to rewards. They noted striking anatomical differences between the genders in their fMRI studies—when anticipating an uncertain reward, men showed more activity in the ventral putamen than women. When receiving a reward, women showed more activity than men in the anterior medial prefrontal cortex.

On a molecular level, Becker's team has found noteworthy gender differences in the concentration and location of receptors for the neurotransmitter dopamine, which is crucial to modulating phenomena of anticipation and reward.<sup>4</sup> For instance, the female hormone estradiol enhances dopamine release among women. "Since the effect of estradiol is seen only in females," she said, "this mechanism may offer unique pharmacological opportunities for the treatment of drug abuse in women."

The presence of cocaine tends to dampen normal gender differences in response to stress, craving, and relaxation, reported Marc N. Potenza MD, PhD, associate professor, and colleagues in the department of psychiatry at Yale University, New Haven, Conn.<sup>5</sup> This was largely due to an increase among cocaine-dependent women in activation of the corticolimbic circuitry involved in stress and craving. Potenza's research team did not notice this increase among men or among women who were not cocaine-dependent.

Grella, who was not present at the APA's annual meeting, said she is not aware of any direct applications of this kind of research to the pharmacology of addiction. But she added that it has "tremendous potential" to inform relapse-prevention strategies that would be more specific to women.

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## References

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