

## **GENDER DIFFERENCES AND SUBSTANCE DEPENDENCE**

### **Prevalence**

Men are 2-3 times more likely to develop drug abuse/dependence disorder than women. Alcohol use disorder can be found 4 times more often in men. Abuse of illicit substances is dominated by men (6.5% women versus 10.0% men), while it has to be found that the non-medical use of prescription drugs is comparable between men and women (2.6% women versus 2.7% men) (National Survey on Drug Use and Health, 2003).

### **Pharmacokinetics, Pharmacodynamics**

A variety of physiological factors lead to gender-specific differences in response to substances in terms of their effects and side effects. These include weight, ratio of fat to water in the body, transporter proteins in the cells, metabolizing enzymes, and hormones.

### **Pharmacogenomics**

Genetic differences that affect the individual's disease or response to a drug are often tied to single polymorphism or mutation. Such mutations are usually not carried on X-chromosome making them independent from gender. However, they can be modified by sex hormones.

### **Medication Research**

Women were largely excluded from clinical trials because of the possibility of pregnancy resulting in birth defects and hormonal fluctuations caused by the menstrual cycle and menopause. This was the case until 1993, when the American Food and Drug Administration (FDA) reversed course on including women in trials and implemented special safety measures. This kind of research is more expensive, mainly because of additional factors that influence metabolism and must be evaluated. Today, the prototype for the research of new medications is no longer the male gender.

### **Different Hypothesis**

“Women are expressive-hypothesis”: Women are more sensitive and emotional in regard to diseases. Female patients attend appointments with physicians more often. Psychotropic medications are prescribed to women more often.

“Substitution hypothesis”: Gender different coping strategies regarding stress and anxiety. Women tend to use medications, while men prefer using alcohol.

“Convergence hypothesis” (“male dominated culture”): Medication use decreases and more alcohol used by women as they assimilate in the male dominated culture and fall into “male” patterns of coping.

### **Comorbidity**

Women have a higher rate of comorbid psychiatric disorders (19.4%), anxiety (46.8%), attention-deficit/hyperactivity disorder (ADHD) (19%) and borderline personality disorders and PTSD (45%). (Callaly et al., 2001; Schubiner et al., 2000; McCance-Katz et al., 1999; Deykin et al., 1997). The male to female ratio of anxiety and major depression is 1:2.

### **Lifestyle**

The close friends and/or partners of dependent women often suffer from addiction problems as well. Interpersonal relationships may be chaotic. Women with addictions often have experienced and/or continue to be subjected to physical and/or sexual abuse. Poor coping strategies are observed.

### **Age of Onset**

Women tend to be older when they start substance abuse.

## **Course**

Disease progression in alcohol dependent women is reported to be faster than in men. Somatic vulnerability, which is manifested in organ damage (liver, brain, heart, etc.), is higher in female alcoholics.

## **Consumption patterns**

Women tend to consume lower levels of alcohol or nicotine, binge less often, and have shorter periods of abstinence.

## **Mortality**

Though women live to be older, their average life span without considerable disability is 72 years compared to 69 years for men. The highest mortality rate can be found in the male population from 20 to 40 years of age (drug and/or alcohol related accidents). The mortality rate of people who abuse illegal substances is 13-17 times higher than that of the general population (Hickmann et al., 2003).

## **Treatment**

Women who abuse or are addicted to substances are less likely to seek treatment than men. If they do seek treatment, women are more likely to choose psychiatric facilities. In general, women have a higher treatment drop out rate. However, if they enter earlier in their addiction, they show comparable retention rates.

## **Stigmatization and Socio-economic Disadvantage**

Generally, women are more deeply affected by stigmatization and socio-economic disadvantages. Female addiction patients often failed to finish their education, have inferior jobs and fewer prospects for the future. Child custody issues raise central problems for women with children and their ability to raise their children is questioned by authorities and society as a whole. Women show lower educational levels, poorer job perspectives, and more employment problems than their male counterparts.

## **GENDER DIFFERENCES IN REGARD TO DIFFERENT SUBSTANCES**

### **Nicotine**

A growing number of adolescent women abuse nicotine. Among females age 14 to 24, nicotine dependence lies at 18.5%, while 19.1% of men are diagnosed as nicotine dependent. Women smoke fewer cigarettes and more "light" products. Metabolism of nicotine is faster in women than in men. Cotinine (a metabolite of nicotine) levels are lower in women. A special issue for women is the regulation of their weight via smoking (WHO, 1992). Women are more likely to rely on cigarettes to cope with stress and negative emotions (Danielsson et al., 1999; File et al., 2001). They tend to relapse in situation involving negative emotions, conflicts and stress, while men tend to relapse in positive situations, such as social events (Heatherton et al., 1991). In regard to long-term effects of smoking, female smokers show lower fertility, enter menopause 2-3 year earlier, and have a higher incidence of osteoporosis (Action on Smoking and Health, 1999). Smoking during pregnancy has negative effects on the fetus and neonate (reduction of placental blood flow, neonatal abstinence syndrome, low birth weight, etc.).

### **Alcohol**

An American study found that 62% of men (over 18 years of age) and 46% of women reported frequent alcohol consumption. According to the WHO one of five males and one out

of twelve females develop alcohol dependence. An increasing prevalence rates can be observed, especially in female adolescents as the rates of consumption even out between the sexes. In 2003, 9.1% of women and 8.7% of men, age 12 to 17 years reported consumption of alcohol or illicit substances in a study by the American National Survey on Drug Use and Health. Though men still dominate in the abuse of illegal substances (6.5% of women vs. 10% of men), it is important to mention that the rate of use is level between the sexes regarding the non-medical use of prescribed medications (2.6% of women vs. 2.7% of men).

### **Cannabis**

The most frequently used illicit substance in Europe is Cannabis. Three to thirty-one percent of the adult population (age 15-64 years) has smoked cannabis at least once. Lifetime prevalence in Europe lies between 10 and 25% (EMCDDA, 2005). The UNODC report of a prevalence of cannabis abuse between 0.8% and 11.3 %, in the European population aged 15-64 years and shows figures for US at 12.6%, Australia at 13.3%, Asia between 0.004 – 6.4% and Africa between 0.05 – 21.5 % in the general population (World Drug Report, 2006).

### **Amphetamines, LSD and Other Synthetic Substances**

Lifetime prevalence of use in the general adult population (age 15-64 years) lies between 0.1% and 6%. In Great Britain, 12% is reported (EMCDDA, 2005).

### **Cocaine and Crack**

Recent national demographical data on Europe reports that 0.5% to 6% of the population consumed cocaine at least once in their life (lifetime-prevalence) (EMCDDA, 2005). Interestingly, a comparable cocaine-induced cerebral vasoconstriction is shown in men and women in the gestagen phase of menstrual cycle (Kaufman et al., 2001). Another study showed that in the follicular phase the psychomotorically activating effect is greater (Roth, 2004).

### **Heroin and Other Opioids**

The EMCDDA report estimates that between 2 and 10 persons per 1000 (respectively 1% of the population) shows a problematic consumption of heroin (EMCDDA, 2005). The male: female ratio lies at 3:1. Women show higher density of my-opioid receptors but implications as to the tolerated doses has yet to be more thoroughly explored (Zubieta et al., 1991). Women show higher risk behavior and higher rates of medical problems (e.g. thrombophlebitis, abscesses, amenorrhea). More than 30% of women in treatment facilities are of childbearing age. Pregnancy is a main issue in the treatment of dependent female patients. A diversified opioid agonist treatment may lead to neonatal abstinence syndrome in neonates. Neonates of mothers in stable treatment setting have better outcomes.