

UZALEŻNIENIA LEKOWE: MECHANIZMY NEUROBIOLOGICZNE I PODSTAWY FARMAKOTERAPII*

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DRUG DEPENDENCE: NEUROBIOLOGICAL MECHANISMS AND PHARMACOTHERAPY
ABSTRACT – Drug dependence is a complex disorder of the central nervous system, characterized by a compulsion to seek and use the drug in question (craving). It is a chronic disorder in which relapses may occur even after long periods of abstinence. Dependence is linked to disturbances in functions of the reward system as well as in the emotional, cognitive and activating systems. The brain reward system controls the basic appetitive behaviors, directed towards profitable and subjectively rewarding stimuli. Crucial to the functioning of the brain reward system is dopamine, particularly dopaminergic neurons in the limbic structures. Dopamine is released from these neurons especially during the first (unexpected) contact with rewarding stimuli. When the stimuli begin to be applied repeatedly, tolerance develops. It has been shown, however, that tolerance to the pharmacological rewards (such as drugs of abuse) does not develop as well as towards natural rewards. Dopamine is also involved in associative learning and in the transfer of rewarding properties from primary rewards onto conditioning signals (conditioned rewards). It is interesting that cocaine does not lose its rewarding properties in mice devoid of dopamine transporter. This proves that dopamine is not the only neurotransmitter involved in reward and dependence processes. Significant role may be played here by other neurotransmitter systems, such as serotonergic, noradrenergic, and peptidergic (e.g. peptide CART – Cocaine and Amphetamine Regulated Transcripts). Important role in pharmacotherapy of drug dependence may be played by substances which act upon dopaminergic system, for example, partial agonists (such as BP897), antagonists of calcium channel L, NMDA antagonists, GABA-ergic agents and preparations affecting the opioid system. Acamprosate and naltrexone are currently considered most important in treatment of alcoholism, while enzymatic antibodies and vaccines generate a lot of interest in treatment of cocaine dependence.

Key words: dependence, reward system, craving, relapse, dopamine, pharmacotherapy.

WSTĘP

Najbardziej niebezpieczną cechą substancji psychoaktywnych jest ich zdolność do wywołania uzależnienia. Uzależnienie lekowe należy traktować jako złożoną chorobę ośrodkowego układu nerwowego, charakteryzującą się natrętnym, niekiedy niekon-

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