nicznie alkohol. Uzyskano dwie linie zwierząt, jedna nosi nazwę Warsaw High Preferring (WHP) i druga Warsaw LOW Preferring (WLP), w których szczury wykazują wysoką preferencję do alkoholu powyżej 5g/kg/24h (WHP) i niską poniżej 1-2g/kg/24h (WLP).

Zwierzęta obu linii były badane behawioralnie i biochemicznie na poziom alkoholu we krwi i stężenie neuroprzekaźników w poszczególnych strukturach mózgu. W 11 pokoleniu szczurów WHP i WLP średni czas trwania snu wynosił 100 min dla (WHP) i 184 min dla (WLP) po podaniu dootrzewnowym (I.P.) 5,0 g/kg etanolu.

Stężenie alkoholu we krwi po podaniu I.P. 2g/kg etanolu było wyższe u szczurów linii WLP niż WHP. Badania biochemiczne wykazały znaczne różnice między obu grupami w stężeniu serotoniny i jej metabolitu kwasu 5-hydroksyindolooctowego, dopaminy i jej metabolitu DOPAC w prążkowiu.

Generalnie, rezultaty badań wskazują na znaczne różnice w biodostępności alkoholu i znaczne różnice w stężeniach neuroprzekaźników w mózgu szczurów linii wysokopreferującej (WHP) i niskopreferującej (WLP) alkohol.

Wanda Dyr, Anna Witanowska, Jolanta Dzierzkowska, Krystyna Iwińska, Paweł Krząścik, Wojciech Kostowski

Biochemical and behavioral analysis of a new line of rats selectively bred for high ethanol consumption

Summary

Studies on the development of an animal model of alcohol dependence have been conducted at the Pharmacology Department of the Institute of Psychiatry and Neurology for many years now. Such models are important in the research on the mechanism underlying alcohol action, the mechanism of dependence formation, as well as on drugs inhibiting this process. Selective breeding of animals for alcohol preference has been accepted and is widely used as a model of experimental alcohol dependence formation (Li et al. 1994). Selective breeding of Wistar rats for voluntary ethanol (EtOH) consumption yielded two lines: the Warsaw High Preferring (WHP) and Warsaw Low Preferring (WLP) rats. The former (WHP) are characterized by a high ethanol consumption (over 5g/kg/24h), while the latter (WLP) - by a low one (below 1-2g/kg/24h).

Both these rat lines were submitted to a behavioral examination as well as to biochemical analysis of blood ethanol and neurotransmitters concentration in particular cerebral structures. In the 11th generation of rats the mean duration of sleep induced by 5,0 g/kg of intraperitoneally administered ethanol (i.p. EtOH) was 100 minutes in WHP and 184 minutes in WLP rats.

Blood ethanol concentration after i.p. administration of 2g/kg EtOH was significantly higher in the WLP line than that in WHP rats. Biochemical analyses have shown significant differences between the two lines in the brain concentration of striatal serotonin (5-HT) and its metabolite, 5-HIAA, as well as striatal dopamine

(DA) and its metabolite, DOPAC. Generally, obtained results indicate marked differences between the WHP (high ethanol preferring) and WLP (low ethanol preferring) rats as regards EtOH bioavailability and brain concentration of neurotransmitters.

Key words: ethanol / alcohol-preferring rats / blood ethanol / monoamines

PIŚMIENNICTWO

1. Bisaga A., Kostowski W. *Selective breeding of rats differing in voluntary ethanol consumption.* Pol. J. Pharmacol. 1993, 45 431-436.
2. Colombo G., Agabio R., Lobino C., Reali R., Zocchi A., Fadda F., Gessa G.: *Sardinian alcohol-preferring rats: a genetic animal model of anxiety.* Physiology and Behavior 1995, 57, 1181-1185.
3. Dyr W., Dzierzkowska J., Iwińska K., Krząścik P., Witanowska A., Kostowski W. *Preliminary biochemical and behavioral analysis of the new line of rats selectively bred for high ethanol consumption.* Alcohol and Alcoholism, 1997, Vol. 32, No 3, pp. 379
4. Eriksson K.: *Genetic selection for voluntary alcohol consumption in the albino rat.* Science 1968, 159, 739-741.
5. Fadda F., Mosca E., Colombo G., Gessa G.: *Effect of spontaneous ingestion of ethanol on brain dopamine metabolism.* Life Science 1989, 44, 281-287.
6. Fulginiti S., Artinian J., Cabrera R., Contreras P.: *Response to an ethanol challenge dose on sleep time and blood alcohol level in Wistar rats prenatally exposed to ethanol during gestational day 8.* Alcohol 1989, 6, 3, 253-256,
7. Gongwer M., Murphy J., McBride W., Lumeng L., T.-K. Li.: *Regional brain contents of serotonin, dopamin and their metabolites in the selectively bred high-and low-alcohol drinking lines of rats.* Alcohol. Vol. 6, pp. 317-320.
8. Li T.-K., Lumeng L., McBride W., Murphy J.: *Genetic and neurobiological basis of alcohol seeking behavior.* Alcohol and Alcoholism. 1994, 29, 697-700.
9. Lumeng L., HawkinsT., Li T-K.: *New strains of rats with alcohol preference and non-preference.* In Alcohol and Aldehyde Metabolizing System. Vol. 3, Thurman R., Williamson J., Drott H., Chance B. Eds.1977, 537-544, Academic Press, New York.
10. Murphy J., McBride W., Lumeng L., Li T-K.: *Monoamine and metabolite levels in CNS regions of the P line of alcohol-preferring rats after acute and chronic ethanol treatment.* Pharmacol. Biochem. Behav. 1983, 19, 849-856,
11. Murphy J., McBride W., Lumeng L., Li T-K.: *Contents of monoamines in forebrain regions of alcohol-preferring (P) and -nonpreferring (NP) lines of rats.* Pharmacol. Biochem. Behav. 1987, 26, 389-392,
12. Murphy J., McBride W., Gatto G., Lumeng L., Li T-K.: *Effects of acute ethanol administration on monoamine and metabolite content in forebrain regions of ethanol-tolerant and -nontolerant alcohol-preferring (P) rats.* Pharmacol. Biochem. Behav. 1988, 29, 169-174.
13. Spanagel R., Montkowski A., Allinham K., Stohr T., Shoaib M., Holsboer F., Landgraf R.: *Anxiety: a potential predictor of vulnerability to the initiation of ethanol self-administration*