REVIEW OF CLINICAL PHARMACOLOGY AND
PHARMACOKINETICS, INTERNATIONAL
EDITION 18: 182 (2004)

The Anxiolytic Profile and the Withdrawal Effects of Chlordiazepoxide Evaluated in the BKW and C57BL/6J Mice

Carolina StavroulaTsitsirigou[1,2] and Alison Bratt[1]

[1]School of Pharmacy and Biomolecular Sciences, Department of Pharmacology, University of Brighton, U.K.; [2]School of Medicine, Department of Pharmacology, University of Thessaly, Larisa, Greece

Benzodiazepines are the most widely prescribed drugs. Chronic treatment with benzodiazepines leads, occasionally, to dependence, while cessation of the therapy results in a withdrawal syndrome mainly characterised by anxiety. In addition, their pharmacological effects differ between individuals. The aim of this study was to investigate the involvement of genetic substrates in the regulation of the action of benzodiazepines. The anxiolytic effects of acute administration of Chlordiazepoxide (CPD) were studied and the withdrawal effects of the agent were assessed after sub-chronic treatment in C57BL/6J and BKW mice on the elevated plus-maze (EPM). The animals were first exposed undrugged on the EPM and exhibited a significant strain difference in their behaviour, with BKW strain displaying higher levels of anxiety. Acute treatment with 10mg/kg and 20mg/kg CPD caused sedation in the C57BL/6J and anxiolysis in the BKW but the high dose presented an overlapping sedation as well. Chronic treatment with CPD (10mg/kg/day x 14 days) produced withdrawal in the BKW mice (anxiogenesis). C57BL/6J mice did show anxiogenic behaviour. Finally, the effect of repeated maze exposures and handling/i.p. injection was investigated by comparing the recordings obtained from the control animals of the study. This study suggests that genetics play a role on the emergence of anxiety disorders and underlie the sensitivity to benzodiazepine treatment and the withdrawal syndrome.