Mouse strain differences in sensitivity towards anxiolytic drugs, a telemetric study

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In search for mechanisms that underlie anxiety processes, mice are often the species of choice to investigate the role of specific receptors or neurotransmitters in anxiety disorders, because of the available mutants technology. It is widely acknowledged that mouse strain differences exist in behavioural traits involved in stress and anxiety as well as differences in pharmacological sensitivity to anxiolytic drugs. One receptor knockout model for anxiety, the 5-HT_{1A} knockout mouse (1AKO) has been generated in three strains of mice, 129 Sv/Ev, Swiss Webster (SW) and C57BL/6J. In order to compare these strains of 1AKO mice and to investigate mechanisms responsible for the differences that are found, knowledge of sensitivity towards anxiolytic drugs of their background strains is of great importance. To this end, mice of these strains were studied in the stress-induced hyperthermia (SIH) test, using telemetric measurements of body temperature (BT), heart rate (HR) and locomotor activity (LA). Exposure to a stressor (rectal temperature measurement) results in autonomic responses, i.e. hyperthermia. Anxiolytic drugs injected 60 minutes before the stressor have the ability to reduce this hyperthermia. The following anxiolytic drugs, affecting the serotonergic or GABA-ergic system were tested: diazepam (1, 2, 4 mg/kg), 5-carboxamido-tryptamine (5-CT; 0.5, 1.0, 2.0 mg/kg) and flesinoxan (0.3, 1.0, 3.0 mg/kg). The anxiolytics diazepam and flesinoxan reduced SIH in all strains, C57 mice being the least sensitive. As expected, in all strains the 5-HT_7 agonist 5-CT had an effect on basal BT but no anxiolytic. These data indicate that mice of different strains show differences in their sensitivity towards anxiolytic drugs in the SIH paradigm. When using receptor knockout animals in anxiety research the differential responses of wildtype mice have to be considered, as they may reflect differences in neuronal systems, including receptors and enzymes.

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