

## Effects of diazepam on $^{125}\text{I}$ -iomazenil-benzodiazepine receptor binding and epileptic seizures in the El mouse

Nobuyoshi FUKUMITSU,\* Shigeyuki OGI,\*\* Mayuki UCHIYAMA\*\* and Yutaka MORI\*\*

\*Proton Medical Research Center, University of Tsukuba

\*\*Department of Radiology, The Jikei University School of Medicine

**Objective:** To investigate changes in free benzodiazepine receptor density in response to repeated, long-term administration of diazepam in epilepsy, we assessed  $^{125}\text{I}$ -iomazenil ( $^{125}\text{I}$ -IMZ) binding in a mouse model. **Methods:** El mice were divided into two groups of 12 mice each which received either no diazepam (El(D[−]) group) or 2 mg/kg of diazepam per week (El(D[+]) group). Nine ddY mice were used as a control. Once each week from the age of 5 to 19 weeks, the El mice received stimulation to produce epileptic seizures 20 minutes after receiving intraperitoneal injections. At 20 weeks of age, a total dose of 0.37 MBq of  $^{125}\text{I}$ -IMZ was injected in all mice and their brains were rapidly removed 3 hours later. The incidence of epileptic seizures at the age of 19 weeks and the autoradiograms of the brain were compared. **Results:** The incidence of epileptic seizures in response to weekly stimulation was significantly lower in the El(D[+]) group than in the El(D[−]) group ( $p < 0.001$ ). The percent injected doses of  $^{125}\text{I}$ -IMZ per gram of tissue in the cortex, hippocampus and amygdala were significantly lower in the El(D[+]) group than in the El(D[−]) group ( $p < 0.05$ ). **Conclusion:** The results suggest that diazepam binds competitively to  $^{125}\text{I}$ -IMZ as an agonist to free benzodiazepine receptor sites in the cortex, hippocampus and amygdala and shows anticonvulsant effect in El mice.

**Key words:**  $^{125}\text{I}$ -iomazenil, benzodiazepine receptor, epileptic seizure, diazepam, El mouse