

## ROLE OF GABAB RECEPTORS IN THE BALANCE OF EPILEPTIC AND PSYCHOTIC-LIKE PHENOMENA IN DBA/2J MICE

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Gamma-amino-butyric acid (GABA)<sub>B</sub> receptors play a key role in the pathophysiology of psychotic disorders and epileptic phenomena (1). We previously reported that baclofen, the prototypical GABA<sub>B</sub> agonist, elicits antipsychotic-like effects in the rat paradigm of prepulse inhibition (PPI) of the startle, a highly validated animal model of schizophrenia (2). Thus, in the present study we studied the role of GABA<sub>B</sub> receptors in the spontaneous PPI deficits displayed by DBA/2J mice, a seizure-susceptible strain. Baclofen (1.25-5 mg/kg, i.p.) dose-dependently restored PPI deficit in DBA/2J mice, in a fashion similar to the antipsychotic clozapine (5 mg/kg, i.p.), and induced a simultaneous precipitation of spontaneous seizures. Pre-treatment with the GABA<sub>B</sub> antagonist SCH50211 (50 mg/kg, i.p.) reversed both effects. In contrast, baclofen did not affect either PPI or EEG activity in C57BL/6J mice. Finally, quantitative autoradiographic analyses assessed a lower GABA<sub>B</sub> receptor expression in DBA/2J mice in comparison to C57BL/6J controls in prefrontal cortex and hippocampus, but not in other brain regions. Our data highlight GABA<sub>B</sub> receptors as an important substrate for sensorimotor gating control and epileptogenesis in DBA/2J mice, and encourage further investigations on the role of GABA<sub>B</sub> receptors in sensorimotor gating, as well as in the reciprocal interplays between psychotic disturbances and epileptic phenomena.

(1) Mizukami K., Ishikawa M., Idaka S., Iwakiri M., Sasaki M. and Iritani S. (2002)  
*Prog Neuropsychopharmacol Biol Psychiatry*. 2:393-6

(2) Bortolato M., Frau R., Aru GN., Orrù M. and Gessa GL. (2004)  
*Psychopharmacology*. 3:322-330