33° Congresso Nazionale della Società Italiana di Farmacologia Cagliari, 6-9 Giugno 2007

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

<u>Bortolato Marco¹</u>, Frau Roberto², Orrù Marco², Piras Anna Paola², Gessa Gian Luigi², Castelli Maria Paola², Mereu Giampaolo³, Marrosu Francesco¹

Gamma-amino-butyric acid (GABA)B receptors play a key role in the pathophysiology of psychotic disorders and epileptic phenomena (1). We previously reported that baclofen, the prototypical GABAB 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 GABAB receptors in the spontaneous PPI deficits displayed by DBA/2J mice, a seizure-susceptible strain. Baclofen (1.25-5 mg/kg, i.p.) dosedependently 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 GABAB 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 GABAB 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 GABAB receptors as an important substrate for sensorimotor gating control and epileptogenesis in DBA/2J mice, and encourage further investigations on the role of GABAB 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

¹Dept. of Cardiovascular and Neurological Science. University of Cagliari, Cagliari, Italy

²Dept. of Neuroscience "Bernard B. Brodie". University of Cagliari, Cagliari, Italy

³Dept. of Experimental Biology "B.Loddo". University of Cagliari, Cagliari, Italy