47- ROLE OF PROLACTIN IN THE ANTI-DIABETIC EFFECTS OF BROMOCRIPTINE: POSSIBLE ACTION THROUGH ESTROGEN RECEPTOR ALPHA IN THE BRAIN

Isadora C Furigo[1], Miriam F Suzuki[2] , João AB Pedroso[1], Angela M Ramos-Lobo[1], Amanda Alencar[1], Daniella C Buonfiglio[1], Pryscila D. Teixeira[1], Thaís T Zampieri[1], Gabriel Orefice[1], João E Oliveira[2], Paolo Bartolini[2], Carlos RJ Soares[2], Jose Donato Jr.[1]

[1]Department of Physiology and Biophysics, Institute of Biomedical Sciences, University of Sao Paulo, Sao Paulo, Brazil, [2] Biotechnology Center, Nuclear and Energy Research Institute – IPEN, CNEN/SP, Sao Paulo, Brazil

The quick release bromocriptine mesylate (Cycloset®) was recently approved as a drug to treat type 2 diabetes mellitus, but the exact mechanism of action of this drug remains unknown. Aims: We hypothesized that the anti-diabetic effects of bromocriptine is due to reductions in basal prolactin levels. Furthermore, these effects could be mediated by an interaction with estrogen receptor α (ERα) in the brain. Methodology: Initially, we studied 4 groups of obese and diabetic (*ob/ob*) mice for 16 days: 1) control; 2) prolactin (micro-osmotic pumps infusing prolactin; 18 µg/day); 3) bromocriptine (one daily ip injection of bromocriptine mesylate; 12 µg/g); and 4) bromocriptine + prolactin. Results: No changes in food intake were observed among the groups; however, bromocriptine groups showed a reduced weight gain along the experiment. Prolactin replacement prevented the improvement in glucose tolerance, insulin sensitivity and serum insulin levels caused by bromocriptine treatment. In another experiment, we found that ERα mRNA showed a very high co-expression with prolactin-responsive cells in hypothalamic nuclei involved in the regulation of glucose homeostasis, such as the arcuate and ventromedial nuclei. Conclusion: Our results suggest that changes in basal prolactin levels are at least partially responsible for the anti-diabetic effects of bromocriptine. These effects are possibly mediated by a crosstalk between prolactin and ERα signaling in the brain. Our findings revealed a novel mechanism that could be target of drugs to prevent and treat diabetes mellitus.

Keywords: ob/ob mice, type 2 diabetes mellitus, dopaminergic agonist, metabolism, energetic control, central nervous system

Financial Support: Sao Paulo Research Foundation (FAPESP-Brazil)