2015

Bardoxolone methyl: a potential therapeutic for the prevention of anti-psychotic drug-induced obesity?

Danielle Camer
University of Wollongong, dc608@uowmail.edu.au

Christopher Bell
University of Wollongong, cjb692@uowmail.edu.au

Yinghua Yu
University of Wollongong, yinghua@uow.edu.au

Alexander M. Szabo
University of Wollongong, aszabo@uow.edu.au

Francesca Fernandez-Enright
University of Wollongong, fernande@uow.edu.au

See next page for additional authors

Publication Details

Camer, D., Bell, C. J., Yu, Y., Szabo, A., Fernandez, F., Dinh, H. C. & Huang, X. F. (2015). Bardoxolone methyl: a potential therapeutic for the prevention of anti-psychotic drug-induced obesity?. Proceedings of 22nd Multidisciplinary ISBS International Neuroscience and Biological Psychiatry "Stress and Behavior" Conference (pp. 22-22).

Bardoxolone methyl: a potential therapeutic for the prevention of anti-psychotic drug-induced obesity?

Abstract
Abstract of a presentation.

Disciplines
Medicine and Health Sciences

Publication Details
Camer, D., Bell, C. J., Yu, Y., Szabo, A., Fernandez, F., Dinh, H. C. & Huang, X. F. (2015). Bardoxolone methyl: a potential therapeutic for the prevention of anti-psychotic drug-induced obesity?. Proceedings of 22nd Multidisciplinary ISBS International Neuroscience and Biological Psychiatry "Stress and Behavior" Conference (pp. 22-22).

Authors
Danielle Camer, Christopher Bell, Yinghua Yu, Alexander M. Szabo, Francesca Fernandez-Enright, Hoang Lan Chi Dinh, and Xu-Feng Huang

BARDOXOLONE METHYL: A POTENTIAL THERAPEUTIC FOR THE PREVENTION OF ANTI-PSYCHOTIC DRUG-INDUCED OBESITY? D Camer, CJ Bell, Y Yu, A Szabo, F Fernandez, CHL Dinh, and XF Huang, Centre for Translational Neuroscience, School of Medicine, University of Wollongong and Illawarra Health and Illawarra Health and Medical Research Institute, Wollongong, ANSTO LifeSciences, Australian Nuclear Science and Technology Organisation, NSW, Faculty of Social Sciences, University of Wollongong, Wollongong, NSW, Australia, Schizophrenia Research Institute, Sydney, NSW, Australia

INTRODUCTION: Antipsychotic drug treatment is known to cause obesity in psychiatric patients. Recently, a derivative of oleanolic acid, bardoxolone methyl (BM) has been shown to have therapeutic benefits in reducing inflammation, a key contributing factor to the development of obesity. However, effects of BM on the development of obesity and associated comorbidities have not been studied. **METHODS:** C57BL/6J male mice were fed a lab chow (LC) (5% of energy as fat), HF (40% of energy as fat), or HF diet supplemented with 10 mg/kg/day BM orally for 21 weeks. Novel object recognition testing was performed to assess recognition memory. Signaling molecules including inflammatory mediators were examined via western blotting in the hypothalamus and prefrontal cortex of mice. **RESULTS AND DISCUSSION:** BM administration prevented HF diet-induced obesity by preventing increases in food intake, body weight, hyperleptinemia, and hyperinsulemia in mice fed a HF diet ($p<0.05$). In the hypothalamus, BM administration prevented HF diet-induced impairments to leptin signaling by modulating energy balance regulation molecules involved in downstream JAK2-Akt-FOXO1 signaling and prevented increases in inflammatory mediators such as TNFα and PTP1B. In addition, BM treatment prevented HF diet-induced decline in recognition memory ($p<0.001$). In the prefrontal cortex of HF diet fed mice, BM administration improved downstream BDNF-TrkB-Akt signaling and prevented HF diet-induced increases in the protein levels of inflammatory molecules, pJNK and PTP1B ($p<0.05$). These results identify a potential novel application for BM in preventing HF diet-induced obesity and associated comorbidities. Furthermore, preliminary testing in antipsychotic-treated rats indicates a potential therapeutic capacity of BM to prevent antipsychotic-induced obesity. **RESEARCH SUPPORT:** This research was supported by Diabetes Australia.