Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol16Issue1abst124P.pdf

Effects of D-Galactose insulin tolerance, serum lipids and renal function: A Comparison between young mice treated with D-Galactose and 24 months old mice

W. Hull[1], W. Chadwick[2], K. Brown[2], S. McSweeny[2], D. Bedford[2], C. Theimermann[1.] [1]Translational Medicine and Therapeutics, William Harvey Research Institute, London, UNITED KINGDOM, [2]Takeda Cambridge Ltd, Cambridge, UNITED KINGDOM

Introduction. D-Galactose (D-Gal) has long been used in neurological research to mimic the effects of ageing in mice. Administration of D-Gal for 6 weeks reduces the performance in many cognitive tests(1), possibly due to increased formation of free radicals and advanced glycation end-products (2). There is little information about the effects of chronic D-Gal administration on systemic metabolic function. In this investigation the effects of D-Gal administration on metabolic and renal function are explored.

Methods. C57/BL6J mice either a) aged for 24 months or b) administered D-Gal or water orally for 10 weeks. At 10 weeks of D-Gal administration animals were sacrificed by CO_2 and exsanguinated by cardiac puncture. Data is presented as mean ± standard error and was analysed by Student's t-test or one-way ANOVA followed by Bonferoni's post hoc test, with a P-value of ≤0.05 being considered significant.

Results. When the lean/fat composition of vehicle treated mice (8.122, n=12) is compared to that of old mice (3.937, n=14), there is a clear decrease in lean mass compared to fat, whereas D-Gal mice (7.505, n=12) show no significant decrease in this parameter. When challenged with glucose (OGTT) after a 24h fasting period, the insulin levels of old mice (AUC 41.03, n=12) were significantly higher than those of young mice (AUC 13.62, n=12) with vehicle or D-Gal (AUC 12.32, n=12). Similarly, the fall in blood glucose in response to a challenge with insulin (0.75U/Kg, I.P.) was significantly reduced in old mice (AUC 9037, n=12) when compared to those of young mice that had received either vehicle (AUC 5216, n=12) or D-Gal (AUC 6003, n=12). These data indicate that old mice, but not young mice that had received D-Gal, have a significant degree of insulin resistance. Increases in serum creatinine often reflect an impairment in renal function. When serum creatinine is normalised against lean mass to account for differences in muscle mass with age, there is an increase in serum creatinine in old mice (3.17mg/g, n=10) when compared to young mice (2.463mg/g, n=11) that had received vehicle.

Conclusions. In conclusion, age leads to insulin resistance, changes in fat distribution and a moderate impairment in renal function, however administration of D-Gal does not lead to insulin resistance and fat changes, but does cause an impairment in renal function.

References

1. Wei H. et. al. (2005). *Behavioural Brain Research.* **157(2):** 245-251.
2. Song X. et. al. (1999). *Mechanisms of Ageing and Dev.* **108:** 239-251.