

## Developmental origins of health and disease: can exercise early in postnatal life improve adult outcomes?

G.K. McConell, Institute of Sport, Exercise and Active Living (ISEAL), College of Sport and Exercise Science, Victoria University, Melbourne, VIC 8001, Australia.

Early life (conception, pregnancy, infancy and childhood) environmental factors program fetal and child growth and development with long-term consequences for later health and disease risk, the Developmental Origins of Health and Disease (DOHaD) concept. At least 18% of diabetes prevalence can be accounted for by intrauterine growth restriction (IUGR) which results in reduced pancreatic  $\beta$ -cell mass and insulin resistance in adulthood. Poor placental function is responsible for the majority of clinical IUGR in developed countries like Australia. In addition, having an obese father or mother increases the risks of metabolic dysfunction in offspring. The percentage of couples of reproductive age who are overweight or obese is increasing to such an extent that it is the predominant situation in many countries including Australia.

Because prevention of IUGR remains difficult, developing interventions in the offspring to prevent diabetes after IUGR is important. In addition, although improving diet and increased physical activity in the obese mother before and during pregnancy or in the obese father prior to conception can be protective for the offspring, this strategy is likely to be limited by poor adherence to lifestyle interventions in adults. Therefore, again, interventions in offspring are important.

In a retrospective study of >1400 adults, indirect measures of higher rates of physical activity in children or adolescents were associated with lower rates of T2D and hypertension in adulthood (Fernandes & Zanesco, 2010). Also, children in the highest quartile of moderate-to-vigorous physical activity at 5 y old had lower fat mass at 8 and 11 y compared with those in the lowest activity quartile, even if they returned to a sedentary lifestyle. Early life exercise also protects susceptible rats against obesity and metabolic disease in later life. In rats that develop diet-induced obesity when fed a high fat diet, three weeks of relatively low intensity exercise training immediately after weaning prevented the onset of obesity for  $\geq 10$  weeks after exercise training finished (Patterson, Dunn-Meynell & Levin, 2008). Similarly, exercise from 7 to 15 weeks of age completely protected obesity- and diabetes- prone Otsuka-Long-Evans-Tokushima Fatty rats from developing diabetes at 28 weeks old (Shim *et al.*, 1996).

Remarkably, we found that exercise early in life (from 5-9 weeks) normalized  $\beta$ -cell mass at 6 months of age in IUGR Wistar-Kyoto rats, despite no exercise being performed after 9 weeks of age (Laker *et al.*, 2011). This was despite the fact that there was only a modest increase in  $\beta$ -cell mass in IUGR rats at 9 weeks of age, immediately after the exercise training, and  $\beta$ -cell mass at this age was not restored to that of control rats (Laker *et al.*, 2011). We have also now extended this work to show that exercise early in life (from 5 weeks of age until 9 weeks of age) can overcome some of the negative effects of paternal obesity on *ex vivo* insulin-stimulated skeletal muscle glucose uptake and increase skeletal muscle mitochondrial function in female adult progeny.

Fernandes RA & Zanesco A. (2010). Early physical activity promotes lower prevalence of chronic diseases in adulthood. *Hypertens Res* **33**, 926-931.

Laker RC, Gallo LA, Wlodek ME, Siebel AL, Wadley G & McConell GK. (2011). Short-term exercise training early in life restores deficits in pancreatic beta-cell mass associated with growth restriction in adult male rats. *Am J Physiol Endocrinol Metab* **301**, E931-940.

Patterson CM, Dunn-Meynell AA & Levin BE (2008). Three weeks of early-onset exercise prolongs obesity resistance in DIO rats after exercise cessation. *Am J Physiol Regul Integr Comp Physiol* **294**, R290-301.

Shima K, Shi K, Mizuno A, Sano T, Ishida K & Noma Y. (1996). Exercise training has a long-lasting effect on prevention of non-insulin-dependent diabetes mellitus in Otsuka-Long-Evans-Tokushima Fatty rats. *Metabolism* **45**, 475-480.