

Exercise before conception – dads matter too

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There is an increasing awareness that preconception health of the parents is an important determinant not just in fertility, but also in the health of the pregnancy. Further in rodent models it is clear that paternal health, and in particular obesity perturbs the molecular structure of the sperm altering methylation patterns, modifying the microRNA content as well as increasing oxidative DNA lesions which are transmitted to the embryo. These changes to the sperm ultimately lead to alterations in fetal growth rates *in utero* with smaller offspring, and changes to offspring body weights and composition with female offspring showing a propensity for being obese themselves. Both female and male offspring demonstrate poorer metabolic health, showing signs of glucose intolerance and insulin resistance. This poorer metabolic health was also shown to be transmitted to the second generation, through both maternal and paternal lines.

Intervening in these obese male mice with a mild exercise regime, while maintaining consumption of a high fat diet, prevented any further weight gain and improved lipid/glucose metabolism. This better metabolic health of the male correlated with improvements in their sperm function and normalized the sperm microRNA profile to that of healthy weight males. When these males were subsequently mated, there were improvements in fertility rates, increased fertilization and enhanced development of the early embryo which translated into increased pregnancy and implantation rates. Preconception exercise in these obese males also restored fetal weights to the levels seen for healthy weight males. These improvements in pregnancy outcomes correlated with paternal measures of glycemia, insulin action and serum lipids. Preconception exercise in the males resulted in offspring with improved metabolic parameters. Glucose and insulin metabolism returned to normal in female offspring with reductions in adipose tissue depots and reductions in adipocyte cell size restoring measures to that of offspring from healthy weight males.

These data suggest that interventions aimed at improving paternal metabolic health prior to conception in an obese male can restore the molecular signals in the sperm resulting in improved offspring health. Thereby, suggesting that this window of intervention in males has the capacity to short circuit the amplification cycle of obesity from one generation to the next.