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COMMENT ON LAKER ET AL.

Exercise Prevents Maternal High-Fat Diet–Induced Hypermethylation of the *Pgc-1 α* Gene and Age-Dependent Metabolic Dysfunction in the Offspring. *Diabetes* 2014;63:1605–1611

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With great interest, we read the excellent study by Laker et al. (1) in this issue of *Diabetes*. The authors showed that exercise in mice on a high-fat diet, corresponding to “an unhealthy maternal lifestyle” scenario, can counteract the negative effects of diet-induced obesity through a metabolic pathway in the offspring in mice. Specifically, Laker et al. provided evidence that voluntary wheel exercise spanning 6 weeks prior to and throughout pregnancy reduces DNA methylation of *Pgc-1 α* in muscle but not in the liver. Intriguingly, they also found that this lower methylation persisted into adulthood and that *Pgc-1 α* mRNA was significantly higher in muscle of the exercised group compared with the groups fed the chow and the high-fat diet. *Pgc-1 α* is a master regulator of mitochondrial biogenesis and function of muscle (2), and methylation of this gene has been found to be sensitive to even very short bouts of high-intensity exercise in humans (3). However, while Laker et al. provide important insight into the parent-offspring transmission of metabolic traits, some issues are in need of additional investigation. For instance, does it matter when the exercise is initiated, i.e., would it be enough to exercise only prior to or during pregnancy, or are both required to produce the observed metabolic changes in the offspring? Additionally, a recent study in mice has shown that the female offspring of obese male rats develop metabolic dysfunction, such as an impaired postprandial glucose tolerance (4).

Thus, another important issue is to investigate if strictly paternal, as well as maternal, lifestyle, or both, drives the methylation changes of *Pgc-1 α* in the offspring. Finally, as shown by Barrès et al. (3), could a single bout of exercise of sufficient intensity be enough to produce metabolic effects that carry over to the next generation? Given that U.S. child obesity rates have already reached epidemic proportions, the findings of Laker et al. (1) are of great relevance as they highlight the importance of increasing awareness of how simple modifications of maternal behavior might help reduce the obesity epidemic in children.

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