Adaptations to exercise: the role of epigenetic changes

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DNA methylation is a major epigenetic modification controlling chromatin state and gene expression. In skeletal muscle, adaptations to exercise are driven by gene expression changes, resulting in an improved metabolic efficiency, oxidative capacity and contractile activity. The role of DNA methylation in exercise-induced gene expression is unknown. In two separate human cohorts we found acute exercise dramatically decreased DNA methylation at the whole genome level and at gene controlling glucose and lipid metabolism (*PGC-1*α, *PDK4* and *PPAR*-δ). No change in DNA methylation was observed in trained humans 3 days after the last exercise bout of a training programme, suggesting exercise-induced DNA hypomethylation is a transient process. In mice, promoter methylation was markedly decreased in *soleus* after *ex vivo* contraction, suggesting contraction (and not circulating or neuronal factors) is responsible for exercise-induced hypomethylation. In rat myotubes, caffeine-induced gene expression was paralleled by a decrease in DNA methylation. We observed that components of the putative demethylation machinery were activated after caffeine exposure, suggesting exercise-induced DNA hypomethylation activates a demethylation process. Collectively, our results provide evidence that exercise-induced DNA hypomethylation is a transient and dynamic process controlling mRNA synthesis.