Summary

DOI: http://dx.doi.org/10.53043/2347-3894.acam90026

Summary of: Changing Lanes: Seasonal Differences in Cellular Metabolism of Adipocytes in Grizzly Bears (Ursus Arctos Horribilis) (2022)

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Asian Journal of Complementary and Alternative Medicine. Volume 10 Issue 01

Published on: 21/02/2022

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Cite this article as: Hogan HRH, Hutzenbiler B, Robbins C, Jansen H. *Summary of: Changing lanes: seasonal differences in cellular metabolism of adipocytes in grizzly bears (Ursus arctos horribilis) (2022)*. Asian Journal of Complementary and Alternative Medicine, Vol 10(1), 19-19:2022.

Obesity is among the most prevalent of negative health conditions in humans today, leading to a multitude of metabolic pathologies such as type 2 diabetes and chronic hyperglycemia. In the wild, obesity can have similar effects, except in the case of grizzly bears (*Ursus arctos horribilis*). In preparation for hibernation, grizzly bears can reach body fat contents of >40% yet exhibit none of the chronic negative health effects we see in humans of similar body composition. This unique ability to simultaneously maintain high body fat percentages and metabolic health has been a key question plaguing hibernation biologists for decades.

Previous studies have revealed unique cellular differences in grizzly bear adipocytes including differences in insulin resistance, but other aspects of cellular metabolism were not addressed, leaving this in vitro model incomplete.

In our current study, we set out to define cellular metabolic differences – measured via metabolic flux – of adipocytes in vitro, and how much of that difference was due to intrinsic cellular or humoral factors. Using an Agilent Seahorse XFp extracellular analyzer, extracellular acidification rate and oxygen consumption rate were used as proxies for glycolysis and oxidative phosphorylation, respectively, to calculate ATP production rate under varying serum and pharmaceutical conditions.

We found that active season serum resulted in a generally more glycolytic cell (increase in ATP from glycolysis), regardless of cell season. Conversely, hibernation season serum resulted in a dampening of glycolysis (reduction in ATP from glycolysis), regardless of cell season. Exceptions were found when hibernation season cells were grown in active season serum. The resulting cell respiratory control ratio was calculated to be double that of active season cells grown in active season serum, indicating both intrinsic and humoral influences on grizzly bear adipocyte metabolism that are yet to be explained. Our results were confirmed indirectly by measure of extracellular lactate which increased in cells grown in active season serum.

In addition to cellular metabolism, we investigated the function of insulin resistance in the regulation of lipolysis during hibernation. Given lipolysis is inhibited by insulin and stimulated by isoproterenol, we tested this effect on lipolysis, measured by glycerol release, in both active and hibernation season cells grown in their respective serum. We expected to see a reduction in glycerol release after treatment with insulin in active season, but not hibernation season cells, due to the insulin resistance during hibernation. Our findings revealed no measurable effect on glycerol release, suggesting that insulin plays a much smaller role in the regulation of lipolysis during hibernation than previously thought.

Overall, our study found major serum dependent differences between the active and hibernation season in grizzly bear adipocytes. Identification of the responsible serum component(s) is an ongoing journey that has potential to improve the understanding of obesity related diseases found in humans, such as type 2 diabetes and chronic hyperglycemia.