



POSTER NO 9

The Significance of the Regulatory Effect of Liver Glycogen in Human Metabolism

Lavoie, Jean-Marc; Fillion, Yovan; Couturier, Karine; and Corriveau, Pierre; "Evidence that the decrease in liver glycogen is associated with the exercise-induced increase in IGFBP-1", *Journal of Applied Physiology* (May 3, 2002).

SUMMARY

The purpose of the present study was to test the hypothesis that exercise-induced increase in IGFBP-1 is not always linked to a decrease in blood glucose level and to examine if the decreasing levels of liver glycogen during exercise may be associated with the increase in IGFBP-1.

Three groups of rats were submitted to a 70-min treadmill exercise. One group of rats were (sic) normally fed and the two others had their food intake restricted by 50% (1/2 fast) the night before the experiment. One of these two 1/2 fasted groups of rats were infused (iv) with glucose throughout exercise to maintain euglycemia. Exercise in non-infused 1/2 fasted rats, compared to the normally fed rats, resulted in significant lower blood glucose (min 70) and insulin levels, and liver glycogen content, no change in IGF-I, and significant higher increases in FFA, glycerol, β -hydroxybutyrate, and IGFBP-1. Maintenance of euglycemia during exercise in glucose-infused 1/2 fasted rats reduced to a large extent the decrease in insulin levels but only slightly attenuated the lipid response and the IGFBP-1 response seen in non-infused 1/2 fasted rats. Comparisons of all individual liver glycogen and IGFBP-1 values revealed that liver glycogen values were highly ($P < 0.001$) predictive of IGFBP-1 response during exercise ($R = 0.564$).

The present results indicate that IGFBP-1 response during exercise is not always linked to a decrease in plasma glucose and suggest that the increase in IGFBP-1 during exercise may be related to the decrease in liver glycogen content.

EDITOR'S COMMENT

Most of the work on liver glycogen was carried out in the first half of the twentieth century. Over the next five decades, this topic did not generate much scientific interest. This in itself is strange, in so far as liver glycogen is the primary reserve fuel store for the brain. The brain itself has no storage capacity for glucose (brain glucose will last only about 30 seconds under normal conditions). If and when liver glycogen runs low and is not adequately replenished, as during exercise and during the night fast, the brain activates the adrenal glands to release hormones which degrade tissue (mainly muscle protein) to create new glucose as fuel for liver replenishment. This animal study on liver glycogen depletion shows that even when blood glucose is stable, a signal is released from the liver (in the form of Insulin-like Growth Factor Binding Protein-1 or IGFBP-1) to "warn" the brain that trouble is ahead if action is not taken.

Another similar study indicates that IGFBP-1 is also released overnight¹. In this study, the authors state that "insulin-like growth factor binding protein (IGFBP)-1 levels increase overnight, being inversely related to changes in insulin."

The Jean-Marc Lavoie study on exercise clearly shows the relation between liver glycogen plenitude and IGFBP-1 release. This relationship, along with the link in the second study to overnight physiology, indicates that this protein (IGFBP-1) is a stress signal from the liver indicating approaching metabolic danger to the brain, such as when the liver glycogen store is depleted. It is important to note again that the release of IGFBP-1 is independent of blood glucose levels. Liver depletion may occur when blood glucose is stable. In that case, if IGFBP-1 levels were linked only to blood glucose levels, liver depletion would *not* initiate a warning signal to the brain indicating an impending fuel shortage.

These studies underscore the need for selective replenishment of the liver prior to bedtime, especially when the evening meal is consumed much earlier. Honey is an ideal bedtime liver fuel as a tablespoon or two would provide the liver with sufficient fuel to stabilize blood glucose as well as maintain fuel supply to the brain during the eight hours of the night fast and thus reduce the production of the adrenal stress hormones, cortisol and adrenaline, that result over time, in chronic adrenal stress.

¹ Cotterill, AM; Holly, JM; Wass JA; "The regulation of insulin-like growth factor binding protein (IGFBP)-1 during prolonged fasting. *Clinical Endocrinology (Oxford)* 1993 Sep; 39(3):357-62