Insulin Sensitivity, Glucose Metabolism, and Membrane Fluidity in Hypertensive Subjects

To the Editor:

We read with great interest the recent article by Dr Rheaume and colleagues1 dealing with a possible link between insulin sensitivity and carbohydrate metabolism in hypertensive subjects. The results of their study demonstrated that insulin sensitivity at rest was lower and not improved by exercise in hypertensive subjects. In addition, it was shown that glycogen contents in skeletal muscles were higher with a concomitant increase in total glycogen synthase in hypertensive subjects. The authors proposed that increased intramuscular glycogen storage and resynthesis in hypertension may be related to higher insulin levels and may represent compensatory mechanisms for the reduced insulin sensitivity in this condition.

Numerous studies have already shown a relationship between insulin and glucose metabolism. It was demonstrated that metformin, an antihyperglycemic drug that improves insulin sensitivity, acts on the liver to suppress gluconeogenesis by potentiating the effect of insulin.2 On the other hand, glucose transport across the membranes may be strongly influenced by a variety of membrane functions, such as membrane fluidity.3 In a study presented earlier, we investigated a relationship between membrane fluidity of erythrocytes and insulin in hypertensive subjects by means of an electron paramagnetic resonance method.4 The membrane fluidity of erythrocytes was significantly lower in patients with essential hypertension than in normotensive subjects. We showed that the higher the plasma insulin level, the lower the membrane fluidity of erythrocytes. This might indicate that hyperinsulinemia might partially explain the increased intramuscular glycogen storage and resynthesis in hypertension. Therefore, we would like to know whether membrane fluidity and other related membrane physicochemical properties of skeletal muscles that the authors biopsied might be changed in hypertensive subjects compared with normotensive controls. It would be necessary to answer more precisely the relationship between membrane functions and insulin-sensitive glucose transport systems in hypertension.

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Response

We are thankful to Drs Tsuda and Nishio for their letter about our study.1 On the basis of their earlier work in erythrocytes,2 they suggest that “abnormal membrane fluidity [in skeletal muscle cells] associated with hyperinsulinemia might partially explain the increased intramuscular glycogen storage and resynthesis in hypertension.” We are not aware of data on membrane fluidity in skeletal muscles of hypertensive subjects. A change in composition of membrane phospholipids—that can reasonably be expected to affect fluidity—has been reported to be associated with the increased insulin sensitivity found in skeletal muscles after physical training.3 Although Drs Tsuda and Nishio make a most pertinent hypothesis, we would caution that observations made in erythrocytes may not necessarily be valid in skeletal muscles. For instance, skeletal muscle cells are specific targets of insulin action, whereas red blood cells do not appear to be, even though insulin receptors also have been reported in the latter.4 With regard to metformin, in addition to its main effect on hepatic cells, there is evidence that it may also in part exert its antidiabetic action by acting on skeletal muscle cells.5 Nevertheless, the possibility that this effect may be indirect and related to an increase in insulin sensitivity conducive to reduced insulin levels and increased receptor numbers in skeletal muscle cannot be ruled out. In conclusion, the speculation that increased intramuscular glycogen storage and resynthesis in hypertension may be related to changes in membrane fluidity made by Drs Tsuda and Nishio remains an interesting hypothesis, but the evidence presently available suggests that this contribution may be only marginal.

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