DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Alcohol, Drug Abuse, and
Mental Health Administration
National Institute of Mental Health
Intramural Research Program
Bethesda, MD 20205

March 20, 1985

David H. Ingvar, M.D., Ph.D.
Professor, Department of Clinical Neurophysiology
University Hospital
S-221 85 Lund
Sweden

Dear David:

It is not easy to comment briefly about the latest paper of Huang and Veech. In general terms, however, it can be dismissed as an atrocity that is more a reflection on the journal that published it than on the writers. It is a gross example of so-called "scientists" who may be competent in one area, but who get involved in something they know nothing about. It is clear that Huang and Veech know nothing about modeling and the mathematical analysis of models. It is also apparent from the experimental data that they are not getting very precise data. The manuscript is full of internal inconsistencies, errors in the understanding of kinetics, and naivete about mathematical analysis of experimental data. For example:

1) In their Figure 1, in the left hand panel, they draw a linear accumulation of [^{14}C]DG-6-P with time--while in the right hand panel of the same figure they show that the substrate, [^{14}C]DG, is declining with time. Tracer concentrations, as used in these experiments, obey first order kinetics, and any school boy would know that you cannot get a constant rate of product formation with a declining concentration of precursor when first order kinetics apply.

2) Their Figure 4 shows extraordinarily scattered data which makes one worry about their analytical techniques. Even their buddy, Hawkins, has gotten better data than that, and so have we. The curve that they have in that figure was fitted to the sum of 2 exponentials. Why 2 exponentials is not clear. It could have been fitted to any number of equations. The curve clearly does not fit the experimental points and represents only those points that emphasized the authors' preconceived conclusion. A clearly better fit would have been one that would have not decreased with time, but would increase, and this could have been obtained by fitting it to some other equation just as valid. Their fitted curve is arbitrary and ignores the high data points and is clearly a case of the data being twisted to fit a prior conclusion.

We have re-examined and repeated the studies done by Huang and Veech in their previous paper and find that they have committed an awful error (I am not sure it wasn't deliberate). The fraction in which they measured the $^{3}H/^{14}C$ and which they designated as pure glucose, is contaminated with other compounds--which explain their results. If the glucose is purified, then their results are null and void. I am enclosing a preprint of a paper on that subject that we submitted to Science. We have not yet received the results of the review, but a number of expert biochemists have read it and are fully convinced by it.

I hope that this fulfills your need.

With best regards,

Yours sincerely,

Louis Sokoloff, M.D.
Chief, Laboratory of Cerebral Metabolism
National Institute of Mental Health
Building 36, Room 1A05
Bethesda, Maryland 20205

Enclosure

"Re-examination of glucose-6-Phosphatase activity in brain in vivo: No evidence for a futile cycle"

by Nelson, T., Lucignani, G., Atlas, S., Dienel, G.A., and Sokoloff, L.
Submitted to Science 2/5/85

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