The data in Hoskin's comments are taken out of their proper context and present, therefore, a distorted picture. A series of recent observations has revealed that the procedures for a quantitative evaluation of the activity in vivo of the membrane-bound enzyme are inadequate due to many factors of the microenvironment not previously recognized. The difficulties are compounded after exposure to organophosphates. Therefore, the extent of enzyme inhibition in vivo affecting electrical activity in tissues after their exposure to organophosphates is at present unknown. However, in several instances the electrical activity of conducting fibers, irreversibly blocked by organophosphates, has been restored by PAM. Whatever the extent of the enzyme inhibition may have been, these observations support the assumption of its essential role since PAM specifically reactivates the enzyme. Similarly, physostigmine, as postulated by electrophysiologists, should first potentiate electrical activity, just as at synaptic junctions, and that is actually observed at the nodes of Ranvier in 10^{-6} to $10^{-5}M$. This is a more sensitive test for the role of the enzyme in conduction than the total block, which may be a complex process requiring high outside concentrations.

Neither the difficulty in establishing a quantitative relationship between the in vivo activity of the enzyme and the electrical activity, nor the failure to dissociate the two activities are considered as "a proof that the two activities are directly associated." But they cannot be used as an argument against the theory. The theory proposed for the role of acetylcholine in excitable membranes is based not on a single fact but on a vast number of data established over three decades. Not one of the facts mentioned by Hoskin contradicts the theory. As in all theories of biological mechanisms, there remain many unsolved problems. The questions raised are discussed in great detail in a forthcoming handbook article (*1*).

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Reference

1. D. Nachmansohn, in *Handbook of Sensory Physiology*, W. R. Loewenstein, Ed. (Springer-Verlag, New York, 1970), vol. 1, pp. 18–102.

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Work Demands or Food Deprivation?

Carder and Berkowitz concluded that rats will work for food in the presence of free food, provided that the work demands are not too high. Although this conclusion may be valid, I don't think it necessarily follows from the evidence presented because, in their experimental procedures, Carder and Berkowitz failed to consider the possibility that food deprivation ("hunger" if you will) was confounded with work demands.

Essentially, their experimental procedure was as follows. Several rats were individually trained to bar-press for food under a reinforcement schedule in which every second response produced a pellet of food (FR2). After two training sessions, free food was made available in the experimental chamber for two test sessions. Generally speaking, the rats continued to respond on the FR2 schedule to obtain food rather than to partake of the free food. In the following two sessions, with the free food removed, the rats were trained under a schedule in which every tenth response produced food (FR-10). Finally, two test sessions were conducted in which free food was again made available. This time, however, without exception the rats preferred to eat the free food rather than earn their food on the FR10 schedule.

During these training and testing sessions, which were 1 hour and 15 minutes and 1 hour long, respectively, the rats had to obtain their entire daily ration of food, because no food was provided outside of the experimental chamber. Under such conditions, it seems quite likely that the rats were not able to obtain as many food pellets during the FR10 training as they did during the FR2 training, simply because the training sessions were so short (1 hour and 15 minutes) and the extended-ratio, bar-pressing experience was so limited (2 days). Thus, the FR10 trained rats would have been much "hungrier" during the test sessions when free food was introduced, and for this reason would have been more eager to eat the free food.

If this reasoning is correct (and no evidence was presented to the contrary), then perhaps work demands may be less important than food deprivation in determining whether a rat will work for food in the presence of free food. And as one thinks about this possibility one begins to wonder whether any animal, rat or man, would work very diligently in a food factory if on the verge of starvation.

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Reference

1. B. Carder and K. Berkowitz, *Science* **167**, 1273 (1970).

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MacDonald raises an important question when he suggests that deprivation may influence the rat's preference for earned, in comparison with free, food. As yet we have not completed a systematic investigation of this influence.

The data, however, do not support his contention that our rats were hungrier during testing with FR10 than with FR2. The session of 1 hour and 15 minutes gave the subjects ample time to earn their daily ration even under an FR10 schedule. Thus on FR2 training sessions prior to free food tests the six rats earned an average of 290 pellets, while on FR10 training sessions the rats earned an average of 282 pellets. Three of the rats earned more on FR2 training sessions while the other three earned more on FR10. This difference cannot account for the fact that all six rats showed a reduced preference for earned food under FR10.

It might be argued, however, that the rats were, for some reason, hungrier during FR10 testing than during FR2 testing, in spite of the fact that they had received equivalent amounts of food before each type of test. If this had been the case, we would expect the rats to eat more pellets, whether free or earned, during FR10 testing. Actually the six rats ate an average of 304 pellets on FR2 tests and 307 pellets on FR10 tests. Again the data fail to suggest a significant difference in hunger under the two conditions.

In the spirit of MacDonald's comment, we would point out that a job can be undesirable even if it pays a living wage.

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