AGEING

Exploring the effect of diet composition in calorie restriction interventions

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Calorie restriction interventions have been shown to increase longevity in animal models and could be beneficial for human health and longevity. What has remained unclear, however, is whether diet composition in calorie restriction paradigms can affect the beneficial effects observed on longevity. Now, new research indicates that daily fasting has a beneficial effect on health and survival of mice independent of calories consumed and diet composition.

"We have been working on two studies of calorie restriction in non-human primates for over 30 years and while the results on the two sites (the University of Wisconsin and the National Institute on Aging) are fascinating, they are reaching two distinct outcomes in terms of survival," explains corresponding author Rafael de Cabo. At the University of Wisconsin the animals on calorie restriction are outliving the animals fed ad libitum, while at the National Institute on Aging, both ad libitum and calorie restriction animals are living for similar lengths of time.

"One of the main differences between the two sites is the composition of the diet, and that is the basis of this paper," adds de Cabo. "In this study, we wanted to test, in mice, whether the two differences in diet composition would lead to the two distinct outcomes in terms of survival."

In the present study, de Cabo and colleagues divided male mice into two diet groups — one group received the sucrose-rich diet that was fed to primates at the University of Wisconsin and the other received the low-sucrose diet that was fed that to primates at the National Institute on Aging. Mice within each diet group were then separated into one of three diet paradigms: ad libitum feeding, 30% calorie restriction and single-meal feeding, which was introduced to control for calorific differences between the two diets. "We found that daily fasting has a powerful beneficial effect on health and survival of mice, independent of calories and diet composition," explains de Cabo.

Next, the authors investigated whether the composition of diet and calorie restriction were associated with metabolic changes in vivo in mice that were 10 months old. The authors found that the respiratory exchange ratio, which is based on an analysis of the amount of carbon dioxide produced and oxygen consumed, in the ad libitum group fluctuated by only a small amount between the light and dark cycles, irrespective of diet. In the 30% calorie restriction and single-meal feeding groups, however, the authors noted large fluctuations in the respiratory exchange ratio upon feeding, and again, these findings were irrespective of diet. The author's note that the large fluctuations observed in mice in the 30% calorie restriction and single-meal feeding groups are consistent with high metabolic flexibility.

Finally, the authors investigated the effect of diet composition and calorie restriction on insulin sensitivity. de Cabo and colleagues used HOMA-IR to determine circulating levels of glucose and insulin in mice that had been fed on their respective diet for 6 months in each of the feeding paradigms. Mice in the 30% calorie restriction group had marked improvements in insulin sensitivity independent of diet composition, whereas no differences were observed for glucoregulatory parameters between mice in the other groups.

"It is promising and provocative to think that time-restricted feeding has such a profound effect on long-term health and survival, and that it seems like a feasible intervention to translate into a clinical setting," concludes de Cabo. "We now need to figure out how to use it as a tool." The team now plan to conduct time-restricted feeding studies using both sexes and different strains and species.

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