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EDITORIAL

Can dietary restriction increase longevity in all species, particularly in human beings? Introduction to a debate among experts

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Abstract This article introduces a special issue of *Biogerontology*, for which a number of international experts who are still active or have been active in research on the effects of dietary restriction (DR) were asked to answer the following question. Do you think that DR can increase longevity in all species, particularly in human beings? Twelve scientists responded with their opinion articles of which roughly half of them taking the position that yes, DR can be applicable to human beings, while the other half arguing for the inapplicability of DR to humans. The conclusions of these learned opinions are summarized here.

Keywords Aging · Non-human primates · Rodents · Flies · Nematodes · Caloric restriction · Calories · Stress · Hormesis · Nutrition

Since the highly publicized, and somewhat inadvertent, dietary restriction (DR) experiment in Biosphere-2 (Walford et al. 2002), public at large generally knows that DR can increase longevity in rodents, and wonders whether DR could also do so in human beings. DR experiments carried out in non-human primates for nearly 20 years obviously reinforce such an interest of the lay public. It is thus not totally unexpected that a few persons have decided to test on themselves the advantages (and risks?) of DR (see e.g. http://www.calorierestriction.org/), and that DR procedures for humans are sometimes described in various media. Besides, many people wonder whether DR could, if not increasing longevity, delay aging and prevent age-related pathologies.

Biogerontologists are probably the most qualified persons able to give an informed opinion on this matter, because they are involved in research on aging and longevity. However, the reading of numerous published articles on DR written by various authors does not provide clear answers to the possible effects of DR in human beings and other species not tested so far. We thus thought that the time is ripe for biogerontologists concerned with DR experiments to answer the question: Do you think that DR can increase longevity in all species, particularly in human beings?

Before contacting various experts, we had the feeling that they would be reluctant to express openly their opinion, because only a few data on the DR effects on humans have been collected so far. To our surprise, only one group of authors (Mockett et al.) declared that time was not ripe to imagine what could be the result of implementing DR in human beings. All the other authors who accepted to write for this

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special issue belong to one of the two camps: the ''Pros'' who think that DR, more or less, would be effective in humans, and the ''Cons'' who reach the opposite conclusion. The irony is that, all authors give very sound arguments and present their own opinion as if it were simply the statement of the obvious.

The authors rely on different theoretical assumptions to foresee the possible effects of DR on longevity of human beings. It thus could be said that biogerontology is still in its infancy because different theories co-exist to explain the same facts, as it is usually observed in ''young'' sciences (see Kühn 1962). According to the ''Pros'', there is no reason to consider that humans would not respond to DR, like other species. This group of authors thus thinks that species are similar regarding their response to DR, and the positive effect of DR on longevity is the rule. On the opposite, the ''Cons'' emphasize that DR would have no effect in species with a late age of sexual maturity, small progeny size and long lifespan, contrarily to what is observed in species showing the opposite pattern. This second group of authors thus considers that DR effects would be different in species with different life history strategies (for a review on life history strategies, see Stearns 1992), because evolutionary constraints, which molded these strategies, have also an effect on the way species respond to DR.

These specially invited articles for this issue of *Biogerontology* are published in an alphabetical sequence based on the first-author surname. Here we try to summarize their answers to the question ''do you think that DR can increase longevity in all species, particularly in human beings'', in three categories as follows.

Category 1: Too early to decide

Robin Mockett and colleagues emphasize that DR fails to extend lifespan in the DBA/2 mice strain and argue that experiments in flies (*Musca domestica*, *Drosophila melanogaster*, *Ceratitis capitata*) have not clearly shown, to say the very least, that DR increases longevity in these species. Because DR does not seem to be a universal phenomenon but, rather, is species-specific, it is difficult and too early, if not impossible, to make a prevision about possible effects of DR in human beings.

Category 2: DR CAN work for human beings

Donald Ingram and colleagues ''currently'' think that DR could increase longevity in humans, even if they have shown that DR does not seem to increase longevity in monkeys who were older than 15 years of age at the beginning of the study. However, they emphasize that we will never know for sure because of impracticability of a DR study in humans, and that, beyond a possible increased longevity, an important consequence of DR studies could be to discover compounds mimicking positive effects of DR on aging and diseases.

Edward Masoro thinks that hormesis (see Rattan 2004) is a component of the life-extending action of DR and that all tested species, animals, plants or fungi, show an increased longevity under DR. A few studies have not reported a life extension under DR, for instance in the C57BL/6 mouse strain, but they have not been confirmed. There is thus no reason to think that DR would not work in human beings.

According to Richard Weindruch, DR seems to improve protection against cardiovascular diseases in humans and to increase health span in monkeys. Thus, it is probable that DR will also increase the span of good health and the average longevity in human beings, as it does in many species.

For Craig Wilcox and colleagues, DR already extends longevity in the Okinawan population of Japan. The authors thus argue that human beings could mildly restrict their diet in the hope to observe positive effects on age-related diseases, aging and longevity, but they also argue that adopting a better diet (fruits, vegetables) is of a clear positive effect.

Byung Pal Yu also emphasizes that it is more important to extend functional longevity than simply lifespan. DR suppresses ''oxidative-stress induced, molecular inflammatory processes'' and there is no reason to consider that DR would have different effects in human beings and in other species: DR does work in various animal species, by extending longevity and improving aging, it would/will work in human beings, too.

Category 3: DR CANNOT work for human beings

Relying on the Demetrius' metabolic stability–longevity theory, Bart Braeckman and colleagues think

that DR would have no effect in species with a late age of sexual maturity, small progeny size and long lifespan, contrarily to what is observed in species showing the opposite pattern. A typical species of the first category is *Homo sapiens* while rodents or nematodes belong to the second category.

Sataro Goto emphasizes that, in Japan, the daily energy supply is 2800 kCal, i.e. nearly 20% less than the average of developed countries, and that the mean longevity of Japanese women is only 85 years. An increased longevity in human beings subjected to DR is thus not expected, as shown by this result obtained at a country scale. However, a mild DR applied at late age could lower the risk for cardiovascular diseases, particularly in countries loaded by the obesity epidemic, but not in Japan or other Asian countries where the energy supply is rather low.

Robin Holliday thinks that DR should increase longevity in species with an irregular food supply or breeding, while the contrary is expected in species with a regular food supply and a regular, commonly annual, breeding cycle. Small rodents and small carnivores, as well as hibernating bears, belong to the first category and large herbivores, arborial primates, whales, dolphins, and human beings are representative of the second category of species. Species in this second category can usually migrate to find out new habitats.

Éric Le Bourg also claims that some species can escape from environments suffering from a food shortage while others cannot. The first kind of species does not need to increase longevity when facing such a food shortage since fleeing is possible, while the other species increase longevity, in the hope that living conditions will soon improve. Humans and other species such as flying birds belong to the first category and, in the past, human populations emigrated when facing famine. Therefore, DR would not increase longevity in human beings.

Considering the reaction norms connecting environmental characters and longevity, Jay Phelan and Michael Rose argue that in rodents the reaction norm between caloric intake and longevity is steep, while it is flat in human beings. Relying on quantitative analyses or demographic data, the authors expect as much as a 67% longevity increase in rodents when switching from ad libitum to restricted feeding, but only 7% in human beings.

Daryl Shanley and Tom Kirkwood emphasize that exceptions to life extension under DR have been observed and that an increase in maintenance in response to a food shortage is not necessarily the best strategy. Particularly, large and long-lived species are less sensitive to a short-term food shortage than small and short-lived species, because these last ones can rely on body stores only for a short time. Anyway, even if human beings would respond positively to DR, social and psychological costs of DR could be high.

Conclusion

It is a fascinating aspect of scientific discussion that scientists can reach very opposite conclusions based on the same data, which is again highlighted in the present debate on the applicability of DR to human beings. This is particularly striking when one compares the articles by Sataro Goto (a ''Con'') and that by Craig Wilcox and colleagues (''Pros'') on longevity in Japan. Similarly, some authors emphasize that DR does not seem to work in flies (Le Bourg, Mockett et al.), while others accept that DR increases longevity in ''laboratory organisms, vertebrates and invertebrates'' (Braeckman et al.).

Even if the experts currently have contradictory opinions, one can expect that DR procedures will finally reveal to be of some help to prevent or delay the onset of age-related diseases or increase ''functional longevity'' in terms of improved quality of life and health span in human beings. This debate among experts could reinforce the will of some biogerontologists to plan new DR experiments, but it could also discourage them! We hope that this special issue of *Biogerontology* will favor the debate on the relevance of implementing DR procedures in human beings, and encourage the relevant experiments to be performed to resolve this issue.

References

Kühn TS (1962) The structure of the scientific revolutions. Chicago University Press, Chicago

Rattan SIS (2004) Aging intervention, prevention and therapy through hormesis. J Gerontol Biol Sci 59A:B705–B709

Stearns SC (1992) The evolution of life histories. Oxford University Press, Oxford

Walford RL, Mock D, Verdery R, MacCallum T (2002) Calorie restriction in Biosphere 2: alterations in physiologic, hematologic, hormonal, and biochemical parameters in humans restricted for a 2-year period. J Gerontol Biol Sci 57A:B211–B224