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QUANTIFYING LIFE STYLE IMPACT ON LIFESPAN

Antonello LORENZINI

University of Bologna, Department of Biomedical and Neuromotor Sciences,
Biochemistry Unit, Via Irnerio 48, 40126 Bologna, Italy
e-mail: antonello.lorenzini@unibo.it

ABSTRACT

A healthy diet, physical activity and avoiding dangerous habits such as smoking are effective ways of increasing health and lifespan. Although a significant portion of the world's population still suffers from malnutrition, especially children, the most common causes of death in the world today are non-communicable diseases. Overweight and obesity significantly increase the relative risk for the most relevant non communicable diseases: cardiovascular disease, type II diabetes and some cancers. Childhood overweight also seems to increase the likelihood of disease in adulthood through epigenetic mechanisms. This worrisome trend now termed "globesity" will deeply impact society unless preventive strategies are put into effect. Researchers of the basic biology of aging have clearly established that animals with short lifespans live longer when their diet is calorie restricted. Although similar experiments carried on rhesus monkeys, a longer-lived species more closely related to humans, yielded mixed results, overall the available scientific data suggest that keeping the body mass index in the "normal" range will increases the chances of living a longer and healthier life. This can be successfully achieved both by maintaining a healthy diet and by engaging in physical activity. In this review we will try to quantify the relative impact of life style choices on lifespan.

Keywords: *lifestyle, physical activity, child, obesity*

KVANTITATIVNI UČINEK ŽIVLJENJSKEGA SLOGA NA TRAJANJE ŽIVLJENJSKE DOBE

IZVLEČEK

Zdrava prehrana, telesna dejavnost in izogibanje nevarnim navadam, kot je kajenje, so učinkoviti načini za podaljšanje dobe zdravja. Čeprav občutni del svetovne

populacije, ki vključuje predvsem otroke, še vedno trpi zaradi podhranjenosti, pa večina svetovnega prebivalstva danes umira zaradi nenalezljivih bolezni. Prekomerna telesna teža in debelost sta dejavnika, ki znatno povečata relativno tveganje za najbolj izrazite nenalezljive bolezni: bolezni srca in ožilja, sladkorna bolezen tipa II in nekatere vrste raka. Raziskave kažejo, da prekomerna teža v otroštvu dodatno poveča verjetnost za bolezni v poznejši odraslosti, tudi preko epigenetskih mehanizmov. Ta zaskrbljujoč trend, ki ga mnogi opisujejo z besedo "globesity", bo v bodoče globoko vplival na družbo, če ne bomo razvili in uresničili preventivnih strategij. Raziskovalci osnovne biologije staranja s pomočjo preizkusov na živalih s kratko življenjsko dobo jasno ugotavljajo, da prehrana z omejenimi kalorijskimi vrednostmi prinaša daljšo življenjsko dobo. Čeprav je podoben preizkus, opravljen na opicah rhesus, ki so živali z zelo dolgo življenjsko dobo in zato tesneje povezane s človeško vrsto, prinesel mešane rezultate, so razpoložljivi znanstveni podatki pokazali, da je potrebno indeks telesne mase ohraniti v mejah »normalnih« vrednosti, da bi povečali možnosti za daljšo zdravo življenjsko dobo. To je mogoče uspešno doseči z zdravo prehrano in s telesno dejavnostjo. V sledeči analizi bomo poskušali oceniti relativne vplive izbire življenjskega sloga na dolžino zdrave življenjske dobe.

Ključne besede: *življenski slog, fizična aktivnost, otroci, debelost*

INTRODUCTION

In biomedical sciences it is usually said that phenotype is the result of the interaction between *genotype* and *environment.* There is a vigorous debate regarding which of the two has the largest influence, but often the dispute is solved by saying that each counts for 50% of the total. For the present discussion on longevity, a different division of factors able to influence phenotype and consequently, in the long run, our lifespan is proposed: *genes*, *chance* and *life style choices*.

INFLUENCE OF GENES

Explaining the roles of genes on lifespan is relatively easy when one makes the following consideration. In contrast to automobiles or other objects that may be built using different quality materials and may consequently last for longer or shorter periods of time, all the different species are made by the same biochemical building blocks: nucleotides, amino acids, fatty acids, carbohydrates etc. In spite of the same "material" employed by nature, maximum longevity is very different among different species: 4

years for a mouse, 122 years for humans and 210 for the bowhead whale (Carey, 2000) [for more animal data see also the extensive collection of species longevity records available online at The Max Planck Institute for Demographic Research].

These enormous differences are probably to be ascribed to a higher capacity in the cells of long-lived species to detect and repair molecular damage [for example see (Lorenzini et al., 2009; Fink, Roell et al., 2011)]. The more accepted evolutionary theory of aging proposes that these cellular repair mechanisms have been positively selected by evolution in species living in biological niches with relatively low mortality rates [for a more clear description of the evolution of longevity, see (Austad, 1997)].

Genetic differences are of course what makes one species different from another. These also account for human variations in eye colour, height, nose shape and, of course, also longevity. Statistical variance measures the average of the squared distance between each of a set of data points and their mean value. Ljungquist and colleagues, in their interesting analysis of identical and fraternal Swedish twins in our species, have concluded that a maximum of around one third of the variance in longevity is attributable to genetic factors (Ljungquist, Berg, Lanke, McClearn & Pedersen, 1998).

INFLUENCE OF CHANCE

The role of chance on longevity is obvious if we consider that all sorts of accidents may shorten our life span or even abruptly end it. Of course, an unfortunate encounter with a microscopic pathogen such as a virus or a bacterium may also shorten our lifespan. It is obvious that these and many other risks have the capacity to influence the length of our lives, but it also seems obvious that they belong to the category of environmental risks, making the proposed division into three categories (genes, chance and choices) appear redundant. Why should we not unite *chance* and *life style choices* in one unifying category called *environmental influence*? There is strong evidence that chance at the molecular and cellular levels is intimately connected to life and independent of the environment, at least relatively to our capacity to control it. To explain this concept with examples let's think of the lifespans of identical twins. Identical twins may get different diseases or the same disease at different ages (Cook, Schnek & Clark, 1981), and of course they may eventually die at different ages (Ljungquist et al., 1998); they have the same genes, but of course we cannot assume that they live in identical environments: even small differences in food choices, for example, could have a potentially important influence on life span. It is different if we move from humans to rodents. In biomedical science the so called "inbred" strains are very useful research models. These are colonies of mice obtained by crossing brothers and sisters for many generations (usually more than ten) so as to obtain, eventually, a colony of genetically identical rodents. The facilities where these laboratory animals are typically housed probably represent the places where man has reached the highest control of environmental conditions. For their entire lives, these animals are housed in identical cages at

a constant temperature with a cycle of 12 hours of light and 12 hours of darkness, and they eat that same food with all the needed micronutrients. Although their genes are identical and their environment virtually constant, their lifespans still vary dramatically. For example, the first mouse in a colony may die after only 200 days of life, while the last mouse of the same colony may live well beyond 800 days (see for example the survival curve for the YBR/EiJ inbred strain on the web site of the Jackson laboratory, a research organization that also supplies biomedical scientists with animal models). This intrinsic biological aspect of chance is rarely mentioned in the biomedical literature, although two well know gerontologists have dedicated an entire monograph to this subject (Finch, 2000).

INFLUENCE OF LIFE STYLE CHOICES ON LIFESPAN

The dependence of lifespan on lifestyle choices is of course what attracts our attention the most. We cannot choose our parents, and consequently we cannot choose our genes. We cannot, by definition, influence our luck or lack of it; even less are we able to influence the chaotic and random components of the lives of our cells and molecules. But in spite of this, it is still important to make wise lifestyle choices since it seems clear that a significant fraction of our lifespan may depend on them. We will dedicate the rest of this essay to this topic.

LIFE STYLE CHOICES

We can divide lifestyle choices into three general categories: keeping away from danger (or not), choosing healthy food (or not), and being physically active (or not). An easy example of "keeping away from danger" is deciding not to smoke. Of course, a lung cell beginning to divide uncontrollably and eventually ending up in a malignant cancer is a random event, but we may lower the likelihood of this event (or not) by simply choosing to smoke (or not). Jeanne Calment of France has so far been the longest-living person on record. She quit smoking at age 119 because she was too blind to light up a cigarette herself, and too proud to ask someone to do it for her. She eventually died at age 122. What can we say with certainty about her long lifespan? That besides probably having very good longevity genes she was also simply lucky! What to eat and how physically active to be are choices that we have to make every day, and they can have a significant impact on our healthspan and lifespan. During a recent survey conducted at an elementary school in a village near the city of Bologna, Italy, we saw first-hand the direction the Western world has taken in terms of lifestyle (Tiso et al., 2010). Children in the West consume too few fruits and vegetables, and too many of them are not physically active enough. The danger in this aspect of our societies goes beyond the

well-studied psychological conditioning that impacts adult lifestyle choices. In other words, children who are not educated to be active while growing up will probably have higher chances to become sedentary adults later on in life, but this is not all. At a subtle biological level, in fact, this will predispose their bodies to adult obesity and other negative conditions. When obesity is reached during a child's development, it influences the development of the adipose tissue so that when adulthood is reached, the body has a higher number of adipocytes compared to that of an adult whose weight during childhood had been normal (Oscai, Babirak, Dubach, McGarr & Spirakis, 1974; Spalding et al., 2008). The body of an adult with more adipocytes stores fat more efficiently. For this adult, consequently, it will be more difficult to maintain normal weight in our "obesogenic" environment where foods rich in sugar and fat are almost always readily available.

These negative effects of unhealthy lifestyle choices are particularly relevant in the early phase of development where they seem capable of influencing even appetite (Rajia, Chen & Morris, 2010). As stated above, these biological conditions are independent of the better-known psychological conditions. The negative effects of both are cumulative.

CALORIC RESTRICTION AND LONGEVITY

The first official report describing the effects on lifespan of a drastic reduction in calories consumed dates back to 1935. In this seminal report, McCay et al. demonstrated that rats kept at near-starvation would have extended longevity (McCay, Crowell & Maynard, 1935). The restriction in calories is considered by the vast majority of gerontologists to be the most robust non-genetic approach to enhancing healthspan and extending lifespan in many species of animals. So far, biologists have used this approach to extend the lifespan of yeasts, worms, spiders, water fleas, rotifers, fish, birds, dogs and even cows (Pinney, Stephens & Pope, 1972). Although these studies are well known among the scientific community, the general public usually has never heard about the influence of caloric restriction on healthspan and longevity. There are people trying caloric restriction (CR) on themselves, and some have created associations like CR Society International and online groups to share recipes and discuss recent advances in the science of aging and longevity. The key and as yet unanswered question is whether CR will work in humans, and if so, to what extent. In rodents, a 40% reduction in food intake can increase median and maximum lifespan by up to 50%. Could CR have similar an effect in humans? Will CR work even if started only after adulthood is reached? At middle age? These are the most common and relevant questions.

Let see what the science of aging has been able to answer so far. In rodents (the most tested species are mice and rats) the most impressive results are obtained when CR is started during development, but it will work even if stared later on in adulthood, although proportionally, giving an increasingly minor lifespan benefit the later it is

started. But what is the amount of restriction we should endure and what is the amount of life extension we could reasonably expect as humans?

Phelan and Rose propose that the increase in longevity that primates, and therefore also humans, may expect is much less significant than that observed in rodents (Phelan & Rose, 2005). Their prediction states that at best humans will experience a 7% increase in lifespan. Their theory is based on an evaluation of how many energy resources are dedicated by a species to reproduction. At least for gestation and lactation, rodents seem to invest much more energy resources than primates. Consequently, Phelan and Rose (2005) speculate that the metabolic switch that CR is able to trigger diverts much of the energy from the metabolic activities related to reproduction to soma maintenance mechanisms, making these mechanisms more efficient in preserving health and consequently prolonging lifespan significantly. Two major on-going studies are currently being conducted on a long-lived primate, the rhesus monkey. Although many of the monkeys are still alive, the researchers have already published the most probable end results of their studies. In one study, the authors concluded that a 30% CR is able to significantly reduce the age at which animals experience their first age-associated diseases (Colman et al., 2009), but in the other the conclusion is that a similar reduction does not influence healthspan and lifespan significantly (Mattison et al., 2012). Although several interesting considerations can be made about these two studies, which have not used the same design, [for a detailed comparison see an interesting commentary (Austad, 2012)] here we will simply say that the available primates data seems so far to support Phelan and Rose predictions of a limited impact of CR on human longevity. Does this mean that the quantity of food we eat is not an important variable in determining our healthspan? Absoluttely not. It is safe to say that overall the CR data underline the importance of retaining as long as possible a "normal" adult weight. It is well known that body weight tends to increase with age. This is true not only for humans, but also for animals kept in a zoo or a laboratory. CR could exert its effect on longevity by simply preventing overweight and obesity.

QUANTIFYING THE EFFECT OF LIFE STYLE CHOICES ON LONGEVITY

We said above that lifespan is definitely influenced by our genes, but of course we cannot choose our mother and father and consequently we have to keep the genes we have. We also said that random chaotic molecular and cellular events may shorten or prolong our life span completely independently of our genes and of our lifestyle choices. Why, then, should we worry about the influence of our lifestyle choices on our healthspan? How much room is left? How much can our choices actually affect the length of our lives?

A very elegant study sought to answer exactly these questions (Khaw, Wareham, Bingman, Welch, Luben & Day, 2008). Khaw and colleagues followed 20,244 men and

women aged between 45 and 79 years, for an average of 11 years. These scientists then divided the population following a simple design in which they assigned1 point to non-smoking subjects, 1 point to subjects eating 5 or more portions of fruits and vegetables daily, 1 point to subjects who engaged in moderate consumption of alcoholic beverages, 1 point to subjects who undertook at least half an hour of leisure-time physical activity a day or who had jobs requiring physical activity.

The survival rate of this cohort was then observed after dividing the population into groups composed of people receiving 0, or 1, or 2, or, at best, 4 points. People receiving 4 points were, of course, considered the ones making the best life style choices.

The result of this analysis was a survival difference between the "0 point-ers" and the "4 point-ers" of 14 years.

This very interesting analysis considers the lifespan impact of several lifestyle choices: good nutritional habits (lots of fruit and vegetables and not too much alcohol), being physically active, and avoiding at least one dangerous behaviour (smoking), but it does not take into account the nutritional parameter of caloric intake, the importance of which we already underlined when we talked about caloric restriction. To quantify the impact of caloric intake, let us consider the result of a very large meta-analysis in which data was collected from 57 different studies with an impressive total of 900,000 subjects (Whitlock et al., 2009). The authors estimated the lost years due to excess body weight by comparing the average lifespans of obese people (body mass index between 30-35) to that of normal-weight subjects (BMI between 22.5-25). The results are about 3 years for obese women and 4 years for obese men. This estimate was made for people over 35 year of age who reached obesity at around 60 years of age, although similar results were obtained by an analysis of United States lifespan tables that included data from age 20 and up, and all the body mass index categories (Fontaine, Redden, Wang, Westfall & Allison, 2003). Avoiding obesity, therefore, adds 3 or 4 years to the years already gained by making the four previously mentioned healthy life style choices.

CONCLUSION

In conclusion, we will calculate whether it is reasonable to invest in "healthy lifestyle choices" as early as possible in life, as well as whether it makes sense to make these choices for our children and to educate them in "healthy nutrition" and "healthy physical activity".

The data from the studies cited in the previous paragraph suggest that people eating a lot of fruits and vegetables, keeping physically active, and avoiding smoking, obesity and excess alcohol, gained 17-18 extra years of life on average.

The cohorts analysed in these studies included mostly people from Western Europe and North America, born just before the end of the first half of the previous century. Considering that life expectancy at birth in 1950 was 68.2 years in the United States (Grove, 1968) we may reasonably say that good lifestyle choices may account for at least one fourth of the duration of our lives.

The present average life expectancy in the Western world is around 80 years (see the WHO Global Health Observatory online charts), and life expectancy has increased linearly in the last century (Oeppen & Vaupel, 2002) and will probably continue increasing; consequently, one fourth of the average lifespan means 20 years for today's children and will mean even more years for the children of tomorrow. These considerations alone provide sufficient justification for "healthy lifestyle" choices. If to the arguments presented in this paper we were to add a discussion of the "quality of life" and how significantly this can be improved by making healthy lifestyle choices, it would be clear just how easy the decision between healthy living and its opposite, the "enjoy today, don't worry about tomorrow" lifestyle, really is.

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