Abolishing ageing?

The importance of being realistic about the biomedical application of biogerontology and its ethical and social implications

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Abstract

While public awareness of biogerontology as a scientific discipline may be rather low, the biomedical application of basic knowledge on the biology of ageing has recently been welcomed by different scientific institutions such as the Royal Society in the UK. In bioethics, such an application has been discussed in the context of human enhancement. While in this debate utopian goals such as immortality have been highlighted, we believe that the current social context and issues closer at hand have not been given enough attention. This can generate misunderstanding regarding the realistic prospect of biogerontological technologies, and reduce their potential benefit. Therefore we have tried to outline this potential benefit according to a statement by some of the leading representatives of the field. This statement of prominent biogerontologists representing the mainstream of their science will provide a reasonable starting point for what we consider to be a realistic expectation about the state of the art of this science and its progress in the near future. Future research particularly on the future outlook of biogerontology is clearly needed but beyond the scope of this article and not our main interest here. Then we will summarise some of the basic concepts of the biology of ageing, and we will outline ethical and social issues, which we believe will realistically result from its application in the near future. Accordingly, we believe that it is first of all important to address the possible negative impact on images of ageing and existing health inequities.

Introduction

Over the last few decades, biogerontology or the study of the biological basics of ageing and senescence has brought about a tremendous increase in knowledge (see e.g. [1]). In the near future, an application of these research results in the form of medical interventions appears to be likely according to many leading experts in the field [2]. Is the public aware of this development? Not particularly. An online search\(^1\) with the keyword «biogerontology» in the archives of the biggest quality daily newspapers in Germany, the UK, and Switzerland delivered almost no results. The eloquent Cambridge scientist Aubrey de Grey apparently gets more media attention with his promise to «end ageing»\(^3\), as his recent publication has been not given enough attention. This can generate misunderstanding regarding the realistic prospect of biogerontological technologies, and reduce their potential benefit. Therefore we have tried to outline this potential benefit according to a statement by some of the leading representatives of the field. This statement of prominent biogerontologists representing the mainstream of their science will provide a reasonable starting point for what we consider to be a realistic expectation about the state of the art of this science and its progress in the near future. Future research particularly on the future outlook of biogerontology is clearly needed but beyond the scope of this article and not our main interest here. Then we will summarise some of the basic concepts of the biology of ageing, and we will outline ethical and social issues, which we believe will realistically result from its application in the near future. Accordingly, we believe that it is first of all important to address the possible negative impact on images of ageing and existing health inequities.

1 This search has been carried out on http://www.thetimes.co.uk/tto/news/ (4 results for «biogerontology»), http://www.guardian.co.uk/ (1, 34), http://www.spiegel.de (0, 5), http://www.sueddeutsche.de (0, 3), http://www.nzz.ch (0, 3) and http://www.faz.net (2, 1) (all accessed on Jan 6th 2011).


4 As e.g. the report «Beyond Therapy» by the President’s Council on Bioethics shows which is often quoted in the context of the manipulation of human ageing. See http://bioethics.georgetown.edu/pceb/reports/beyondtherapy/ (accessed Jan 11th 2011).
mortality achieved by biomedical means [7, 8]. While answering these questions is certainly intellectually challenging and interesting, such answers may not be sufficient and adequate for an ethical evaluation of a possible application of biogerontology in medicine in the near future. In the worst case, they might even be misleading as concerns and fears about a radical modification of human nature are raised, which are not related to any realistic possibility of this scientific field. We acknowledge that a systematic ethical evaluation and review should consider a broad scope of arguments and ethical theories regarding the general objectives of biogerontology and the ethical and social problems resulting from its possible biomedical application in the current social context in the near future. But focusing on a general objective such as immortality could lead to a misunderstanding about the ethical advantages and disadvantages of biomedical applications closer at hand, and may even lead to a general refutation of the science as a whole. To avoid such misconceptions, we will first outline – as the limited scope of this article allows – some basic concepts of biogerontology as relevant for our purpose, and the goals of the related research which according to the mainstream of the discipline may be achievable in the near future. Secondly, we will then sketch two of the main ethical issues, which will probably be raised if this basic research is translated into medical applications. These will be the promotion of negative images of old age and an increase of existing health inequities. We believe these issues are important because they will concern a huge part of future populations, and because sociological surveys show them as the main concern now.5

The demographic change and a possible «longevity dividend» of biogerontotechnology

All scientific institutions mentioned above emphasise the great potential benefits of biogerontological research and its application in relation to the challenges that the demographic change will generate in the social system (pension insurance, long-term care insurance, health insurance). Population ageing and the increase of older age groups above 65 years is a global phenomenon.6 The German Federal Statistical Office currently estimates that the percentage of 65-year-olds in Germany will rise from 21% in 2010 to 33% by 2050. At the same time, it is predicted that the percentage of the working-age population (20–64 years of age) will dwindle from 61% to 51%.7 Morbidity forecasts predict a corresponding increase in chronic diseases and dependency. As a consequence of this, public expenditure for the related social security systems are predicted to rise sharply if no measures are taken. Based on the numbers from OECD and IWF, the rating agency Standard & Poor estimates the increase alone of state costs in Germany caused by the demographic change for the time frame from 2010 to 2050 will be at 10% of the gross national product.8 A large portion of these additional costs is attributed to the increase in age-related illnesses. For example, the Fritz Beske Institute of health care research calculated a 144% increase in dementia for the time frame from 2007–2050.9

While it is not clear how the current morbidity profile of age groups and thus the overall morbidity burden will develop,10 a positive influence on such morbidity profiles by biomedical innovation is undoubtedly desirable. Therefore biogerontological interventions into the ageing process look highly appealing, not at least to political decision makers. They could not only slow down ageing, but also be a very effective prevention strategy of age-related diseases, thus saving costs for health care and pensions, and enabling people to work longer. In a recently published appeal to increase the research budgets dedicated to biological ageing processes (to 1% of the current annual Medicare spending of the US or 3 billion US dollar), leading biogerontologists presented the outlook of a so-called «longevity dividend», which would supposedly slowing down the ageing process by seven years while simultaneously reducing age-related diseases [2]. This would possibly contribute to the goal of a compression of morbidity, popularised by James Fries in 1980 [12], which for decades has been universally popular among geriatricians and the lay public interested in the issue (see e.g. [13]). To achieve the longevity dividend, treatment could begin at age 40, the health condition of an average 50-year-old would then be comparable to that of an average 43-year-old etc. well into old age. That way, the healthy and vigorous life years and employment as well as the average healthy life span could be prolonged. The authors (S.J. Olshansky, S.J. Perry, R.A. Miller, and Robert Butler) can be considered to represent mainstream of their discipline and some of the most important scientific associations in their field. Therefore, we consider their outlook on the possible results of biogerontology in the near future as a reasonable heuristic starting point for our ethical reflection.

The «longevity dividend», which is basically being promised as a dividend for investing in research, then stands out due to the longer working life and lower

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5 See the parts «Successful ageing?» and «Longevity dividend for all?» of our article. Other issues, e.g., research ethics, are beyond the limited scope of this article. For recent discussions see also [9] and [10].
10 For instance, the issue 5/2010 of the journal Bundesgesundheitsblatt was dedicated to the demographic change and the complexities of estimating the future development of the overall morbidity burden. See also [11].
health-care costs because of age-related diseases. The latter should no longer be studied in an isolated way but always in interdisciplinary cooperation and with a focus on biological ageing. This raises issues concerning research policy, its relevant structures and capacities as well as the funding landscape. The arguments related to the «longevity dividend» may therefore address the political obstacles to investments in the related research, which have been outlined by Richard A. Miller under the keyword «gerontophobia». This is supposed to be a «predisposition to regard ... research on ageing ... as a public menace bound to produce a world filled with nonproductive, chronically disabled, unhappy senior citizens consuming more resources than they produce» ([14], p. 170). The paradigm of «compressed morbidity» seems to be an evident goal to meet «gerontophobia».

Partially based on Harry Moody’s four «scenarios of an ageing society» from 1994 [15], Juengst et al. distinguish compression of morbidity, decelerated ageing, and arrested ageing as the main paradigms of biogerontological aspirations [16, 6]. These paradigms include the possible targets of interventions and the possible main goals. In principle, biomedical interventions resulting from research into ageing itself could either target age-related diseases or biological ageing itself. Possible goals are more healthy life years, prolonging vigorous functioning and appearance, and/or a longer lifespan. The main goals could then be to shorten the period in which older people suffer from age-associated diseases without necessarily extending the average lifespan as currently achieved in developed countries. This would lead to a compression of morbidity, which is obviously an uncontroversial goal. At the other end of the spectrum would be arrested ageing, where biological ageing itself would be the target, and a possibly unlimited extension of the human lifespan in a vigorous state the main goal. This is in the focus of the debate on human enhancement already mentioned above. Whatever the future prospects of this goal might be, at the moment the mainstream of biogerontology as represented by the authors of the «longevity dividend» considers this not as a realistic option. However, it should be noted that the proponents of the «longevity dividend», who could be considered to represent this mainstream, also do not merely embrace the controversial «compression of morbidity» paradigm, but «slower ageing» ([2], p. 11). While they argue for the investment in biogerontological research referring to a possible compression of morbidity, they also stress that the most promising target of the interventions developed by biogerontology are not single age-associated diseases, but biological ageing itself. As a side effect to a more effective prevention of age-associated diseases, the average human lifespan compared to what currently is achieved in the best practice countries would also be prolonged. This prolongation would be slightly bigger than the one that has been calculated by Oshansky at al. in 1990, in the event that cancer and cardiovascular diseases should be eliminated. But it would not be more than the result of the same calculation for the possible elimination of cancer, cardiovascular diseases, stroke, and diabetes altogether [17]. While this would be a moderate case of «decelerated ageing», it would still be exposed to the basic criticisms addressed to this scenario as such, e.g. as already expressed by Juengst et al. The main issues that they already narrowly outline in this context are increasingly negative perceptions of the ageing process which is «pathologised», and a possibly restricted access to the interventions guaranteeing «decelerated ageing». First of all, it is thus important to see which negative conceptions of ageing and the relation of ageing and disease are connected to the basic scientific concepts of the current biology of ageing, and how they might be transferred to medicine and in the consequence to the general public.

A problem of biology now solved: the evolutionary, molecular, and genetic aspect of the biology of ageing

In 1952, Peter Medawar published a now classic article entitled «an unresolved problem of biology» in which he stated that there is no satisfying explanation for the biological ageing process [18]. In 1990, the biologist Zhores Medvedev estimated in an attempt to classify theories on biological ageing that there are more than 300 such theories. He considered a comprehensive, unified theory of biological ageing to be unrealistic [19]. About 16 years later, two volumes were published reporting on biogerontological conferences, at which about 20% of the respective scientific community met. Both volumes began with an article by prominent gerontologists (Robin Holliday and Leonard Hayflick), each with the key message that ageing is no longer an unsolved problem [20, 1]. Despite Medvedev’s scepticism, biogerontology seems to have succeeded in developing a theoretical framework that unites various explanatory approaches. This theoretical framework is provided by Tom Kirkwood’s and Robin Holliday’s disposable soma theory, which has a molecular, a genetic, and an evolutionary-theoretical component [21–23]. At a molecular level, biological ageing is generally defined in a hypothesis for which much evidence has been collected, but which according to the biologist David Gems still needs to be fully confirmed [10], as the accumulation of damaged molecules (e.g., DNA mutations, misfolded and aggregated proteins and glycosylated lipids) that exceed the ability of body’s own maintenance and repair systems, which are responsible for reducing and controlling such molecular damage (see e.g. [24]). Thus, the function of cells, tissues and organs becomes increasingly impaired. This loss of function ultimately results in age-related frailty and diseases, whereby the boundary between these and the normal
ageing process is supposed to become blurred, and the transition is far from understood ([25] and [26], p. 153). Such an unclear boundary between normal and pathological ageing could be cited in an argument for an alleged “pathologisation” of the ageing process in general in the view of current biogerontology. In this view, molecular damage and physical mechanisms of maintenance and repair are complimentary elements of biological ageing. Whereas the biological ageing process, in which molecular damage accumulates, is referred to as senescence, the processes that function in cellular maintenance and repair provide «longevity». As its capacity is limited, itself deteriorating with age or overwhelmed by the accumulation of damaged molecules, senescence allows for the process of biological ageing. Accordingly, this notion of senescence is based on stochastic occurrences that are individually different. Contrary to earlier assumptions, biological ageing is neither genetically programmed nor does it have any function which is selected for during the evolution of a certain species. However, a genetic component is believed to be responsible for longevity and the search for the longevity gene is one of the main areas of current biogerontological research (see e.g. [27]).

The dominant evolutionary-theoretical explanation for the origin of this form of senescence and longevity is made by the aforementioned disposable soma theory. This starts with the observed fact that biological ageing does not occur in most organisms in their natural environment, as they die from external causes such as cold, starvation, or predators. The response of most species to the pressures of mortality in their environment is reproduction. Since physical and natural resources at a particular organism’s disposal are limited, a compromise between reproduction and physical maintenance must be found. To maintain the latter beyond the span of life would be detrimental to reproduction and would therefore be a survival disadvantage. Consequently, the balance between reproduction and natural bodily repair is the result of an evolutionary adaption, and biological ageing is a side effect of this. In this context, Kirkwood also adopted the gene effects formulated by Williams [28] and Medawar [18]. According to Medawar, the effect of selection decreases due to the limited lifespan caused by external factors and thus allows for the passing on of genetic defects that have negative effects in later stages of life (e.g., Huntington’s disease). A complementary explanation was put forward by George C Williams. Some genetically inherited traits that have positive effects early in life may have an opposite effect in later life (antagonistic pleiotropy, e.g., an aggressive immune system). Due to external mortality and short lifespans, these genetic features are either no selective disadvantage or a selective advantage.

On this molecular, genetic and evolutionary theoretical basis, the possibility to influence the ageing process is currently being explored. Since this was successful in various laboratory organisms (yeast, nematodes, fruit flies, mice and rats) (see e.g. [29], p. 18–20 and p. 202–318) and corresponding mechanisms have remained across species boundaries, the supporters of the «longevity dividend» assume that interventions can be developed that could also influence biological ageing and age-related diseases in humans. Possible interventions, so far unproven in clinical trials, are: caloric restriction and drugs that mimic its effect, telomerase, novel antioxidants, gene activation of longevity genes, and others (see e.g. [30, 31, 5], p. 52–54). A very short summary of some assumptions of mainstream biogerontology as derived from the sources named above could be the following one: Biological ageing is not programmed and has no biological function. It is connected to a functional decline and impairment that is at least not easily distinguished from age-associated diseases and if so only to a quantitative degree, but not a qualitative one. As ageing is variable and flexible among species and within the individual organism of one species, it can and has been manipulated in some species and there is no reason to believe that this will be impossible in humans.

Successful ageing?

Unlike in the Anglo-American world, the impact of new biogerontological claims on the societal image of old age has hardly been a topic in scientific and social discourse in Germany. Historical studies on the development of the images of old age show how much they are shaped by biomedical knowledge about ageing [32, 33]. Thus, the question remains as to how the biogerontological notion of ageing as a biological and future medically remediable decline could change the society’s image of old age, thereby changing how individuals and society as a whole deal with ageing. In the Anglo-American debate, critics fear that because of the growing importance of biogerontology the already existing tendencies of negativity, pathologisation and medicalisation of ageing could be scientifically established in an influential way. For instance, medical anthropologist Sharon Kaufman and her colleagues noted in respect to regenerative medicine and the idea that ageing is malleable by biomedical means that «…a major effect of biomedicalization today is that the aged body tends to be viewed now as simultaneously a diseased entity, a site for restoration, and a space for improvement» ([34], p. 736). The geriatric neurologist Peter J Whitehouse and bioethicist Eric Juengst cited the concept of «mild cognitive impairment» to document the threat of pathologisation which would put all ageing people in a medicalisation would reduce the potential and heterogeneity of ageing, as well as its individual-existential,
psychological and societal aspects would become less
important. We believe that this possible implication of biogerontology is important just because aging will not
be abolished and the proliferation of negative images of
old age will therefore be of concern for a huge part
of future populations.

Due to the demographic change, the central meaning of
the image of ageing and how the individual and society
deal with it has been more strongly discussed in Ger-
many. Thus, the commission of experts of the sixth age-
ing report\(^1\) came to the conclusion that despite the
fact that older people are generally healthier today and
have more resources available to them than in past and
despite the gerontological efforts to correct the images
of ageing, very simple and negative images of ageing
often prevail. Experts show for various areas of society
that the prevailing negative images of ageing can inter-
fere with the use of the factual potentials of ageing as
well as the human way of dealing with the limits of age-
ing. Against this background, the commission of ex-
erts declares the reflection on the images of ageing as
an important societal task and recommends that the
people involved in school and adult education and
health care for the elderly should receive and take ad-

Longevity dividend for all?

A recent sociological study in Australia has enquired
the ethical evaluation of possible technologies extend-
ing the human lifespan by retarding ageing. Different
population groups have expressed their concerns, and
a prominent one was a limited access to such technolo-
gies so that only privileged groups in society could ben-
efit from them [39, 40]. If a limited access would be un-
just, this would imply that there would be a duty to
provide equal access to medical interventions which
slow ageing. Such a duty has recently been defended by
the philosopher Colin Farrelly, a strong advocate of the
outlook of the longevity dividend. Farrelly argues that
a duty to retard human ageing and equal access to the
corresponding interventions could be defended as a
part of just health care with support by Norman Daniels’ account of equal opportunity and by Ronald Dworkin’s account of equality of resources. This argumenta-
tion may indeed be convincing: the «longevity dividend»
results from extended functioning, which will be rele-
vant for agency, capabilities and the resources of life
plans, which is relevant to some of the dominant con-
temporary theories of justice from John Rawls and Am-
artya Sen (For an overview see [41], p. 225 and [42],
p. 12–30). For example cognitive functioning, mobility,
and sensual perception could be prevented longer from
age-related decline, which will obviously increase the
opportunity to achieve all kinds of goals.

Whilst it may be difficult to argue against universal ac-
to biogerontechnology, which can be convincingly

1 Sachverständigenkommission des BMFSFJ (Hg.) (2010): Sechster
Bericht zur Lage der älteren Generation in der Bundesrepublik
RedaktionBMFSFJ/Pressestelle/Pdf-Anlagen/sechster-altenbericht,
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2 (2010): Stellungnahme der Bundesregierung zum Bericht der Sach-
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ember 18th 2010), S. XVI.

http://bioethics.georgetown.edu/pcke/transcripts/doc02/session1.

11

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supported by such widely recognised theories of justice, an important point would be how this access would in fact look. This question is not treated in any depth or even rarely asked at all. In order to answer it satisfactorily, firstly arguments for rationing or prioritising health care would have to be considered. Health care rationing is often justified by the prospect of steeply rising costs for new technologies (see e.g. the excellent summary of [43]). If biogerontechnology would add to these costs by expensive and complicated interventions, it would be difficult to finance this technology in the context of public health care, even if this would be general requirement of justice. Existing legal requirements what has to be covered by public health care, at least in Germany, have a clear relation to the treatment of diseases. As noted above, this relation is still unclear in the field of biological ageing. Secondly, the current context of existing health inequalities in old age and their social determinants has to be taken into account. Even if access could be extended, the effects might be limited by social determinants of health such as education or job control. Not everybody may have the opportunity to benefit from a longer employment period, and thus may not enjoy any «longevity benefit».

Conclusion

While in the long run, biogerontological research may indeed lead to biomedical interventions with the potential to change the human condition, this seems to be no realistic prospect for the near future. The same realism would be important in the discussion of the ethical and social implications of this technology. Issues of a non-spiritual immortality or the meaning of finitude for the human existence as manifested during the ageing process may be important. But others should at least not be neglected as has been done so far. Thus it would be important to discuss the connection and independence of biomedical and biological images of ageing on one side and cultural and social ones on the other. This would help biogerontologists to meet the scepticism they face, if confronted with the reproach to foster negative stereotypes about ageing. Further, as it is sometimes assumed that a biomedical intervention into ageing will be simple and widely available, it is important to remember that even if this may be the case (which is by no means clear), many groups in society may still be excluded from the potential benefit that biogerontology and biogerontechnology undoubtedly are able to generate. More and intense interdisciplinary and public debates such as started by the Royal Society and the Academy of Medical Sciences are indispensable to find ways how to best exploit this potential.

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cément été saluées par différentes institutions scientifiques telles que la Royal Society au Royaume-Uni. Dans le domaine de la bioéthique, ces applications ont été discutées dans le contexte de la médecine améliorative. Bien que des objectifs utopiques tels que l’immortalité aient été mis en avant dans ce débat, cependant, nous pensons que le contexte social actuel et des enjeux plus proches du quotidien n’ont pas reçu suffisamment d’attention. Cela peut susciter des malentendus sur les possibilités réalistes de technologies biogérontologiques, et en réduire le bénéfice potentiel. C’est pourquoi nous tentons de décrire ces avantages potentiels, en nous basant sur une déclaration faite par certains des principaux représentants du domaine. Cette déclaration représente le courant dominant actuel de la biogérontologie, et offrira un point de départ raisonnable pour ce que nous considérons comme des attentes réalistes sur l’état actuel des connaissances et des possibilités dans ce domaine, et ses progrès dans un proche avenir. Des recherches ultérieures, en particulier sur les perspectives d’avenir de la biogérontologie, sont clairement nécessaires; mais elles vont au-delà du présent article et ne sont pas notre principal intérêt ici. Nous résumerons ensuite quelques-uns des concepts fondamentaux de la biologie du vieillissement, et nous donnerons un aperçu des questions éthiques et sociales, qui résultent selon nous d’une application réelle de la biogérontologie dans un avenir proche. Sur cette base, nous pensons que les priorités sont de traiter du possible impact négatif sur les images du vieillissement, et sur les inégalités actuelles face à la santé.

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