NUFFIELD COUNCIL ON BIOETHICS

The ethics of ageing research

Note of workshop held on 30 November 2016: 10.30-15.30
28 Bedford Square, London WC1B 3JS

Chair: Julian Hughes, RICE Professor of Old Age Psychiatry, University of Bristol and Deputy Chair of the Nuffield Council on Bioethics

Guest list: see Annex A

Background

1 On 30 November 2016 the Nuffield Council on Bioethics organised a roundtable meeting to identify the ethical and social issues raised by recent developments in research on the biological processes of ageing. The aim of the meeting was to help the Council consider the scope of possible future work on this topic. The Council had previously commissioned a background paper on longevity (by Hans-Jörg Ehni) in November 2015,[1] and went on to discuss the issues raised at its annual 'Forward Look' meeting in May 2016. Following this, the Council decided it would explore these issues further at a roundtable meeting with experts from a wide range of disciplines, including biogerontology, philosophy and ethics, sociology and policy. A list of participants who attended the roundtable meeting is at Annex A. This note reports the comments made by the participants at the meeting. **It should not be assumed that all present agreed with all points made, or that the opinions expressed represent the view of the Nuffield Council.**

A Nuffield Council briefing note, drawing both on the discussions on the day and on the background paper circulated in advance, will be published in due course.

Discussions

Achievements of biogerontology research

2 Ageing can be considered to set in if an organism lives longer than is required by evolution i.e. living beyond an age at which reproduction can take place (also called the 'essential life span' of a species). The evolutionary view is that ageing is the degenerative phase of life. If ageing is occurring faster than necessary, ageing might be thought of as a disease. Biogerontology is a field of research concerned with the biological processes that occur when organisms age and with the potential to intervene in the process. The aim of the majority of academic biogerontology research being carried out around the world is to maintain health and increase quality of life in old age. This is sometimes called the 'health span'. The aim rarely is to increase life span, although it is recognised this might be a by-product.

3 Research in this field has led to a good understanding of biological ageing. All organisms age and ageing is not caused by genetic processes; there is no gene that causes ageing (a common misperception). After the essential life span, the ability of organisms to maintain or improve function decreases. Ageing is in-built into the imperfections of the biological system and involves complex changes at the molecular level which occur in different ways in

1 See http://nuffieldbioethics.org/wp-content/uploads/Background-paper-2016-Longevity.pdf

different individuals, tissues, cells and molecules. These changes are associated with disease and loss of capacity that affects the ability to fight infection or tolerate stress. How changes at the cellular or molecular level relate to changes at the whole individual level is not well understood.

4 Although it is widely accepted that biological ageing cannot be halted altogether, it was recently discovered that it is possible to intervene in the process. The manipulation of genes in microorganisms has been shown to increase life span by three or four times. In mice, life span can be increased by 20-30 per cent. Life span has been the primary outcome measure used in animal studies so far; impacts on other aspects such as behaviour have not been examined yet. This research is already going out of the laboratory and into clinical trials. The TAME (Targeting Ageing with Metformin) clinical trial will soon test the effects of the drug Metformin on the metabolic and cellular processes associated with the development of age-related conditions in people aged over 60 years.[2] Participants at the roundtable meeting suggested that a synopsis of achievements to date in biogerontology research would be a helpful starting point for any future work carried out by the Council.

Reductionist vs holistic approaches to ageing

5 Scientists working in this field have been criticised for reducing ageing to a biological process and, in effect, medicalising it. Many changes occur when a person ages and the presence or absence of disease is not the only aspect of ageing that is important to people, or indeed what might influence their ability to be 'healthy'. Ageing is multidimensional and complex, and there may be far more effective ways of improving health and well-being in old age than developing a drug that slows biological ageing. For example, social attitudes towards older people and other aspects of the environment have a major influence on wellbeing in old age. The use (and abuse) of drugs in care homes, for instance, is an important issue influenced by a mixture of medical, social and other factors. The link between cognitive and physical impairment is not well understood. Services for older people should be organised holistically, which currently does not always occur. Intervening to reduce poverty in childhood or improving educational opportunities may also pay greater dividends than developing a pill for ageing. A mixed approach is likely to be the most successful.

6 The biological view of ageing has infiltrated clinical care and the care of the elderly. Some view this as damaging, in that if people are led to believe ageing is dictated by biological processes that are out of their control, they may feel disempowered and miss out on the potential of other kinds of interventions to maintain health and improve quality of life. The biological view of ageing also may be one reason that, in the past, older people were sometimes denied treatment and excluded from clinical research. Until recently, it was widely thought that it would be futile to include older people in clinical trials, and people over 80 in particular were rarely studied. Trials that have included older people, however, have demonstrated the potential for drug therapy to reduce morbidity in older people.[3] The discovery that biological ageing is amenable to treatment has the potential to change attitudes among the medical profession towards older people.

Future research priorities

7 It is important to ask who is setting the research agenda in this field and whose voices are being privileged. The global pharmaceutical industry is a major driver of research on biological ageing and it is likely that more 'Metformin trials' will follow. Data from genetics research and biometrics is likely to increase knowledge further about how medicines work in different people. There are concerns that increasing health span is not the primary

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2 See https://clinicaltrials.gov/ct2/show/NCT02432287b

3 For example, see Beckett NS, Peters R, Fletcher AE *et al.* (2008) Treatment of Hypertension in Patients 80 Years of Age or Older *New England Journal of Medicine* **358**: 1887-98

objective of commercial research, and that it will not address the problems of old age that people are primarily worried about, such as mobility, incontinence and isolation. Often, solutions to these problems are already available and they do not involve or require biological research, such as improving education, increasing physical activity and reducing life stress. A symptom of specialisation is that any field of research tends to look at only one part of the problem, whereas a joined-up approach would be more successful. In addition, there are multiple difficulties with defining the desired outcomes of biogerontology research, such as 'healthiness' and 'increased well-being'.

Consequences of research on biological ageing

8 If interventions that slowed biological ageing and increased health span became available, the potential consequences for individuals and for society more widely require consideration. People's aspirations and expectations of old age may change, and they may feel judged or guilty if they choose not to take ageing interventions. Many people are already anxious about old age, and developments in genetics and neuroscience that are moving towards the prediction of conditions that may develop later in life, such as dementia, may add to this anxiety. If people with such predictions do not take up preventative interventions, such as an ageing treatment, their entitlement to state care later on may be questioned. If no intervention is available, there is likely to be little benefit to the person of advance knowledge of an age-related disease they may develop, particularly given how uncertain such predictions are likely to be. There may also be implications for insurance of individual choices about whether or not to take up ageing treatments.

9 It is hard to predict what the health effects of intervening in biological ageing will be for individuals. In the past, improved interventions to prevent or treat age-related diseases such as heart disease and cancer and the resulting increases in life expectancy have had knock-on consequences, such as more people having dementia. Ageing interventions may result in compressed morbidity, with people remaining healthy until the last few months of their life, which may or may not be desirable to people.

10 Increased knowledge of the biological processes of ageing, and the fact that it is possible to intervene in these processes, may have the effect of encouraging people to maintain a healthy lifestyle as they get older. Exercise, social interaction and meditation, for example, are all good for health. Demonstrating how this works at a biological level may be helpful.

11 Any benefits of research on biological ageing are likely to be felt unevenly within and across societies, as is the case with much biological and medical research. Poorer people and women are likely to be affected by ageing in different ways. The pharmaceutical industry should consider involving people in developing countries in research on biological ageing and should ensure any treatments that arise from such research are affordable and accessible to people in different countries.

An ethical framework for biogerontology research

12 Biogerontology research currently is taking place without an ethical framework. Key questions concern the ethics of applying medical interventions to healthy people in order to increase quality of life; the ethics of prolonging life without increasing quality of life; the ethics of carrying out clinical trials in this field without involving older people; and what kind of research in this field should public systems be funding. The goals of research and the need to take a holistic approach to improving health and well-being in old age have not been widely agreed upon. The ethical values that are central to biogerontology research and the consequences of living longer and better, such as autonomy, dignity, equity and human identity, have not been elucidated, and the potential impacts of biogerontology research on different populations have not been properly considered. The question of whether ageing is a problem and hence something to be 'fixed' also requires further examination. Some do not

consider that ageing should not mainly be regarded as a degenerative process, given that people often become more knowledgeable and reflective as the years pass.

13 The governance of biogerontology research would benefit from having input from other related fields of research, such as ethical, social and clinical research. Older people themselves need to be consulted to find out what is important to them in terms of quality of life, and they should be included in clinical trials of treatments for ageing. Not only will this ensure the results are relevant to the target population, it could also demonstrate that the treatment brings higher returns than if it is tested on younger people (which should be attractive to the trial sponsor).[4] Any research that has the aim of slowing biological ageing will need to consider the effects of interventions on the different dimensions of the ageing process, or the 'health span' of the person, rather than focussing on narrow outcome measures or specific diseases. It should also consider that the norms of ageing are constantly changing. Results from studies on biological ageing in animals should be applied to humans with caution given that animals do not have moral systems or equivalent social lives.

14 Previous work of the Nuffield Council on Bioethics may be relevant here, such as its report on children and clinical research, and on dementia care. A number of other organisations have carried out work in this area. For example, the World Health Organisation published in May 2016 its *Global strategy and action plan on ageing and health*, which is relevant to the discussion, although it does not mention biogerontology research. The vision of the strategy is a world in which everyone can live a long and healthy life and is underpinned by the following principles: human rights, equity, equality and non-discrimination (particularly on the basis of age), gender equality and intergenerational solidarity. The UK Research Councils and the British Society of Gerontology are also active in debate and policy development in this field.

Summary

15 Biogerontology research is developing interventions intended to increase health span. A by-product of this may be an increase in life span. This kind of research has the potential to bring substantial benefits to individuals, but it also raises a number of ethical questions. For example, should the 'normal' ageing process in healthy people be interfered with? In any case, how is 'health span' to be defined in a manner that is not reductionist? How can the benefits of ageing interventions be fairly distributed? What will be the social consequences of the availability of treatments for ageing, such as changing expectations of old age and pressure to take such treatments? How should biogerontology research be regulated and governed to ensure it is carried out ethically and appropriately, and that the place of such research in the wider promotion of health in old age is more broadly recognised? What are the trade-offs to be made between quantity and quality of life and by what criteria do we decide what might be a good or bad trade-off? Can biogerontology accommodate notions of the good life? The development of an ethical framework for future research in this field would be helpful, and this should involve multidisciplinary input from clinical, social and ethics expertise.

4 For example, see Beckett N, Peters R, Tuomilehto J et al. (2012) Immediate and late benefits of treating very elderly people with hypertension: results from active treatment extension to Hypertension in the Very Elderly randomised controlled trial. *BMJ* 2012;344:d7541

Annex A: Participants

John Beard
Director, Department of Ageing and Life Course, World Health Organization

Ann Gallagher
Professor of Ethics and Care, University of Surrey and a member of the Nuffield Council on Bioethics

Kenneth Howse
James Martin Senior Fellow, Oxford Institute of Population Ageing

Roland Jackson
Visiting Fellow at the Royal Institution (previously Executive Chair of Sciencewise) and a member of the Nuffield Council on Bioethics

Liz Lloyd
Professor of Social Gerontology, Senior Research Fellow, School for Social Care Research, University of Bristol

Mary McCabe
Emeritus Professor of Ancient Philosophy, King's College London

Alisoun Milne
Professor of Social Gerontology and Social Work, University of Kent

Suresh Rattan
Associate Professor, Department of Molecular Biology and Genetics, Aarhus University, Denmark

Helen Small
Professor of English Literature, University of Oxford

Cameron Swift
Emeritus Professor of Health Care of the Elderly, King's College London and Co-convenor, UK Age Research Forum

Anthea Tinker
Professor of Social Gerontology, King's College London

Heather Widdows
John Ferguson Chair of Global Ethics, University of Birmingham and a member of the Nuffield Council on Bioethics

Teresa Williams
Director of Social Research and Policy, Nuffield Foundation

Thomas von Zglinicki
Professor of Cellular Gerontology, Newcastle University

Observers

Emma Fabrega Domenech
Masters student in Social Anthropological Research, University of Manchester

Nuffield Council on Bioethics staff

Hugh Whittall
Director

Catherine Joynson
Assistant Director

Anna Wilkinson
Programme Manager