



**HAL**  
open science

## Stay social, stay young: a bioanthropological outlook on the processes linking sociality and ageing

Vincenzo Iannuzzi, Nicolas Narboux-Nême, Andrea Lehoczki, Giovanni Levi, Cristina Giuliani

### ► To cite this version:

Vincenzo Iannuzzi, Nicolas Narboux-Nême, Andrea Lehoczki, Giovanni Levi, Cristina Giuliani. Stay social, stay young: a bioanthropological outlook on the processes linking sociality and ageing. *Gerontology*, 2024, 10.1007/s11357-024-01416-5 . hal-04785327

**HAL Id: hal-04785327**

**<https://hal.science/hal-04785327v1>**

Submitted on 15 Nov 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



# Stay social, stay young: a bioanthropological outlook on the processes linking sociality and ageing

Vincenzo Iannuzzi · Nicolas Narboux-Nême ·  
Andrea Lehoczki · Giovanni Levi ·  
Cristina Giuliani 

Received: 31 July 2024 / Accepted: 24 October 2024  
© The Author(s) 2024

**Abstract** In modern human societies, social interactions and pro-social behaviours are associated with better individual and collective health, reduced mortality, and increased longevity. Conversely, social isolation is a predictor of shorter lifespan. The biological processes through which sociality affects the ageing process, as well as healthspan and lifespan, are still poorly understood. Unveiling the physiological, neurological, genomic, epigenomic, and evolutionary mechanisms underlying the association between sociality and longevity may open new perspectives to understand how lifespan is determined in a broader socio/evolutionary outlook. Here we summarize evidence showing how social dynamics can

shape the evolution of life history traits through physiological and genetic processes directly or indirectly related to ageing and lifespan. We start by reviewing theories of ageing that incorporate social interactions into their model. Then, we address the link between sociality and lifespan from two separate points of view: (i) considering evidences from comparative evolutionary biology and bioanthropology that demonstrates how sociality contributes to natural variation in lifespan over the course of human evolution and among different human groups in both pre-industrial and post-industrial society, and (ii) discussing the main physiological, neurological, genetic, and epigenetic molecular processes at the interface between sociality and ageing. We highlight that the exposure to chronic social stressors deregulates neurophysiological and immunological pathways and promotes accelerated ageing and thereby reducing lifespan. In conclusion, we describe how sociality and social dynamics are intimately embedded in human biology, influencing healthy ageing and lifespan, and we highlight the need to foster interdisciplinary approaches including social sciences, biological anthropology, human ecology, physiology, and genetics.

**Keywords** Sociality · Ageing · Lifespan · Human evolution · Physiology · Stress

---

V. Iannuzzi · C. Giuliani (✉)  
Laboratory of Molecular Anthropology & Centre  
for Genome Biology, Department of Biological,  
Geological and Environmental Sciences, University  
of Bologna, Via Selmi 3, 40126 Bologna, Italy  
e-mail: cristina.giuliani2@unibo.it

N. Narboux-Nême · G. Levi (✉)  
Physiologie Moléculaire Et Adaptation, CNRS UMR7221,  
Département AVIV, Muséum National d'Histoire  
Naturelle, Paris, France  
e-mail: giovanni.levi@mnhn.fr

A. Lehoczki  
Doctoral College, Health Sciences Program, Semmelweis  
University, Budapest, Hungary

A. Lehoczki  
Institute of Preventive Medicine and Public Health,  
Semmelweis University, Budapest, Hungary

## Introduction

The proportion of elderly individuals is rapidly increasing in the world and is expected to reach about

16% of the population in 2050 [1], exacerbating the burden on the medical system due to the higher prevalence of diseases linked to ageing such as dementia, cardiovascular problems, osteoporosis, and sarcopenia [2]. Sociality is one of the main factors associated with better health and longevity [3]; social isolation has an impact on mortality equivalent to recognized risk factors such as obesity, smoking, lack of physical activity, and poor access to health care [4, 5]. It has been shown that social isolation and loneliness are associated with an increase in the likelihood of mortality of 29% and 26% respectively [6]. It appears that social organization, social interactions, and intergenerational transfer are associated with delayed ageing, reduced mortality, and increased longevity not only in humans but also in other mammals [7–11]. These observations suggest the existence of evolutionary-conserved biological processes associating sociality with longevity. Comprehension of these processes could have profound effects on the understanding of human social dynamics with a direct impact for decision-makers to optimize the support people at this stage of life, for them and society [1].

This review summarizes recent advances in biological anthropology, physiology, epigenetics, and genetics to highlight how the relationship between sociality and biological processes has shaped human lifespan throughout evolutionary history and continues to impact it in contemporary populations (Fig. 1). First, we describe theories of human ageing including social aspects, then we provide insight into bio-anthropological evidence that establishes a connection between sociality and natural variations in lifespan across different timescales. Among various factors, we explore the impact of inter-generational transfer and resource sharing on life history traits of pre-industrial societies and indigenous populations, where the influence of the “modern” environment is reduced. Indeed, extended lifespans are not exclusive to contemporary human life: humans exhibit the longest lifespan among primates, even in conditions characterized by high mortality, such as those experienced by hunter-gatherers. Then, we present an analysis of how social dynamics influences physiological, neurological, and endocrinological processes associated with lifespan determination, providing examples from genetically modified model animals. We show that exposure to chronic social stressors can permanently deregulate neurophysiological and immunological

pathways, promoting accelerated ageing. In conclusion, we describe genetic and epigenetic factors involved in the link between sociality and lifespan and we suggest the use of biomarkers of ageing such as the “epigenetic clocks” in study aimed at investigating the link between sociality and human ageing. We conclude that multidisciplinary approaches including social sciences, biological anthropology, ecology, physiology, and genetics are needed to decipher the multiple facets of an ageing society and to be prepared to face the ongoing demographic shift.

### Theories of human ageing which include social aspects

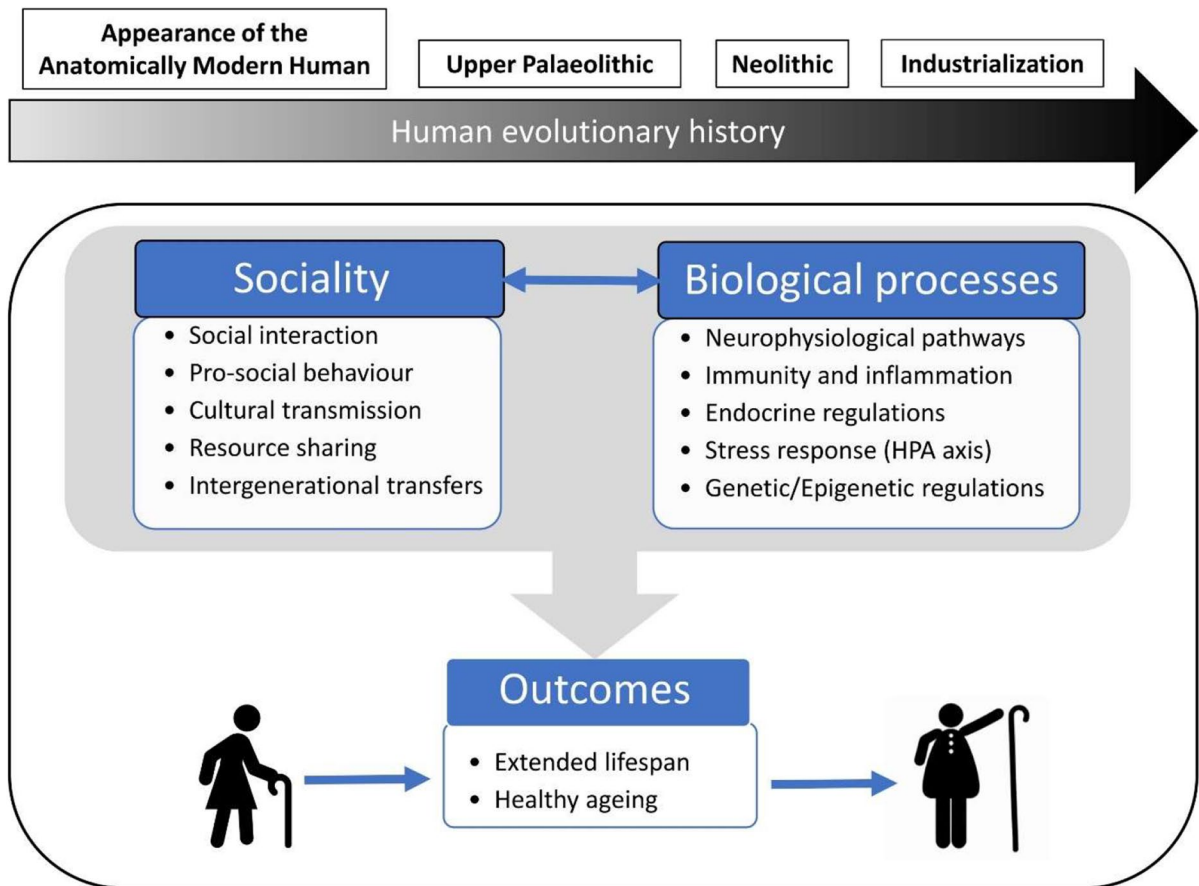
Over 300 theories have been proposed regarding the ageing process [12]—see for example: [13–16]. However, only a few of them integrate the impact of social dynamics or pro-social behaviours or social isolation while these aspects are progressively becoming the central focus in contemporary outlooks to “Geroscience Research” [17].

We begin by discussing major classical theories of ageing which include fundamental social concepts such as intergenerational transfer and resource sharing.

#### Kin selection theory

One of the first attempts to include the social dimension in the study of lifespan extension is the so-called kin-selection theory [18–21]. According to this theory, the lifespan of an individual may negatively or positively affect the fitness of its relatives, creating an additional selective pressure on longevity [22]. In this light, a delayed onset of ageing might increase the quality and the quantity of care provided to the offspring and to the closest relatives, showing that life-history evolution is influenced by inclusive fitness effects. Although the “kin-selection theory” has been questioned for some of its applications [23, 24], it is widely accepted as an explanation for social behaviours observed in many taxa [25–28]. Indeed, the “kin-selection theory” has been widely investigated in eusocial species, in mammals, and in humans.

In the case of eusocial insects, the prediction that reproductive altruism should be directed toward kin



**Fig. 1** Schematic representation of the narrative approach adopted in this review. The approach is based on the analysis of the interplay between sociality and biological processes that are central to the process of healthy ageing and that help

to explain the extended lifespan that is a characteristic of our species. The relationship between these factors has been subject to continuous modulation throughout the course of human evolution

is firmly supported [29]. In ants, for instance, the long living queens caste is an example of a phenotype evolved thanks to kin selection [18, 30, 31]. In fact, the caste system of division of labour between short living sterile workers and long living queens (which share the same genome) allows only the latter to reproduce and thus to pass their genes to the next generation. Since the queen is the sole reproductive individual in these monogynous societies, sterile workers can avoid the demise of the entire colony only by helping their fully fertile relative to survive and reproduce. This leads to strong selection for queen longevity [32, 33].

Kin selection is a driver of longevity also in mammalian species. In a recent study, Zhu and co-workers [34] have performed a comparative phylogenetic

analysis of the longevity of about 1000 mammalian species living in three different modes of social organization: solitary, pair-living, and group-living. Their main finding is that group-living species live longer than solitary species; this result is valid both in terms of “absolute longevity” and of “residual longevity” (after adjustment for body mass). Group-living species may live longer due to reduced risks of predation and/or starvation. Furthermore, in primates, it has been shown that stable social bonds in a group are associated to prolonged lifespan [35–37]. Thus, association among kins can influence coalition in a group, cooperative breeding, and the emergence of social hierarchies which, ultimately, can increase the evolutionary fitness of a social species. This study provides also results from brain transcriptomic

analyses of 94 mammalian species showing that hormonal regulation and immunity constitute a shared mechanism that link social organization and longevity [34]. In view of the biological mechanisms summarized later in this review, this observation is not surprising, it is, however, in the brain that one has to finally find the common genetic regulations that affect social behaviour and longevity.

In humans, the general framework of the kin-selection theory includes also the “grandmother hypothesis” [38], and the “intergenerational transfers” model [39] that Bourke (2007) attempted to reconcile.

### *Grandmother hypothesis*

The “grandmother hypothesis” [38] dates back to the 1960s and was then revised by Hawkes and colleagues [40]. This theory states that extended post-menopausal lifespan coevolved with the mother–child food-sharing habit, a practice that helps elder females to improve their daughters’ fertility and offspring survival. Post-menopausal women help their daughters and nieces to take care of the offspring favouring the nutritional welfare of weaned children, especially when their mother is pregnant again or invested in a task outside the living place. This trans-generational transfer would induce an advantage to reduced senescence, and therefore favour the evolutionary selection of this trait. Grandmothering could favour biological functions related to longevity either through mutation-accumulation or the antagonistic pleiotropy strategies. In the former case, the selection against late deleterious variants is supposed to increase thanks to the contribution of gene pool from long-lived females that increased the reproductive success of their offspring. In the latter, grandmothering would favour mutations that increase adaptive performance at later ages, since it confers fitness benefits through increased alloparental care and reducing, at the same time, reproductive conflict (fertility/senescence trade-off). Empirical evidences of this fertility/senescence trade-off have been found in many studies [41–44] that highlight the role of grandmothering in the evolution of female post-menopausal longevity.

### *Intergenerational transfers model*

In 2003, Lee proposed a biodemographic theory [39], where the use of the social dimension as a

mathematical parameter succeeded to explain the peculiar life-history traits that characterize our species (lower fertility, longer life, increased investments in offspring). This theory generalizes and formalizes the arguments included in the “grandmother hypothesis” by integrating the classical selection due to fertility with the selection due to “intergenerational transfers” across the course of life. The term “intergenerational transfers” refers to the investment of resources in the offspring and other relatives, including parental care and support provided by others, such as grandparents and older siblings. Furthermore, the importance of intergenerational transfers in shaping the ageing patterns has been evidenced also for other social animals [45]. Unlike the classic theories of ageing [15, 16, 38], which claim that natural selection acts weakly at older ages, the model proposed by Lee suggests that selection continues also at older ages since it depends on the investments needed to produce a survivor at a given age. Therefore, selection could also act at post-reproductive ages if it leads to the survival and reproductive success of the juveniles.

### *Life history theory*

Another theoretical framework that includes the social dimension of ageing in complex ecological contexts is the “life history theory” [14, 46–49]. This theory explores how organisms, including humans, allocate their limited resources (such as energy, nutrients, and metabolic processes) across various life-history functions, including reproduction, maintenance, and longevity. The theory starts with the premise that resources are limited. These resources are needed for various life functions, including reproduction, maintenance (e.g. tissue repair, immune function), and somatic survival (longevity). During life, organisms make trade-offs in how they allocate these limited resources. Briefly, the theory suggests that resources allocated to one function (e.g. reproduction) come at the expense of other functions (e.g. maintenance and longevity). For instance, individuals with multiple children may experience a decrease in lifespan due to the energetic costs of pregnancy and childcare [50]. In humans, various cultural, societal, and environmental factors significantly influence personal choices and actions, which can in turn impact the allocation of resources during the life-course.

## Gene-culture coevolution models

Biological anthropology and the study of human evolution provide interesting insight into the complex interdependence between sociality and longevity. Gene-culture coevolution models suggest that social interactions play a crucial role in transmitting cultural and technological knowledge from one generation to the next [51]. According to Gintis (2011), two conditions are necessary for cultural transmission: a brain structure related to social behaviour and an extended lifespan to acquire and transmit cultural knowledge. In this regard, some studies argue that the evolution of genetics of lifespan follows a gene-culture co-evolutionary model with autocatalytic features briefly described below [52, 53]:

- i. cultural practices create selective pressure for genetic variants that are associated with longer lifespan and slower ageing;
- ii. as a consequence, the increase in lifespan leads the elders to have more time available to acquire knowledge and resources to pass on their offspring;
- iii. this promotes further cultural progress, which, in turn, exerts selective pressure on genetic variants that favours a longer lifespan, creating positive feedback.

Studies on great apes support this model [54] and suggest that since during the learning phase the productivity is low, the acquisition of cultural knowledge can happen as long as there are intergenerational transfers from adults to juveniles.

## Embodied capital theory

The embodied capital theory (ECT) [55–57] originated in economics and sociology. It refers to the idea that individuals acquire and accumulate various skills, knowledge, and abilities over their lifetime, which are considered forms of “capital”. This capital, often referred to as “human capital”, represents an individual’s economic value and productivity [56, 58]. This theory has been applied to the study of hunter-gatherer ecologies, and in particular on the knowledge of high-level skills requested to forage high-quality and difficult-to-acquire foods [56], such as meat [59], tubers [60], and honey [61]. Indeed, according to this theory,

the investment in learning extensive foraging techniques generated a return in the form of a dietary shift that, in turn, contributed to the enlargement of human brain capacity and to the evolution of slower human life history traits, such as delayed maturity, and extended lifespan [62].

## Exposome and allostatic load

The concepts of the exposome and allostatic load, as highlighted by Shiels and Stenvinkel, provide a modern theoretical framework to understand how sociality influences longevity [63, 64]. The exposome refers to the full range of environmental exposures throughout an individual’s life, including social factors, nutrition, and the physical environment [63]. Allostatic load reflects the cumulative physiological burden caused by chronic exposure to these stressors, particularly social and environmental challenges [64]. These concepts offer a valuable lens for examining how social structures and interactions shape biological ageing by affecting stress resilience and overall health.

Shiels and Stenvinkel emphasize that chronic stress and socio-environmental pressures, key aspects of the exposome, lead to an accumulation of allostatic load, which accelerates ageing by modulating cellular processes such as inflammation and oxidative stress [63, 64]. In this context, sociality plays a crucial role in mitigating these stressors. Strong social bonds and supportive environments help reduce allostatic load by buffering individuals from chronic stress, thereby protecting against the oxidative stress that drive biological ageing. As a result, these social interactions can slow down ageing and promote longevity; conversely, social isolation and adverse environments exacerbate oxidative stress and allostatic load, accelerating ageing and increasing the risk of age-related diseases such as cardiovascular disease and cancer [65].

## Bioanthropological evidence linking sociality and natural variation in lifespan

In this section, we will show how social dynamics, and in particular intergenerational transfers and resource sharing, may have contributed to the evolution of lifespan variability using evidence from biological anthropology. In this perspective, studying the evolutionary dynamics that connect sociality and

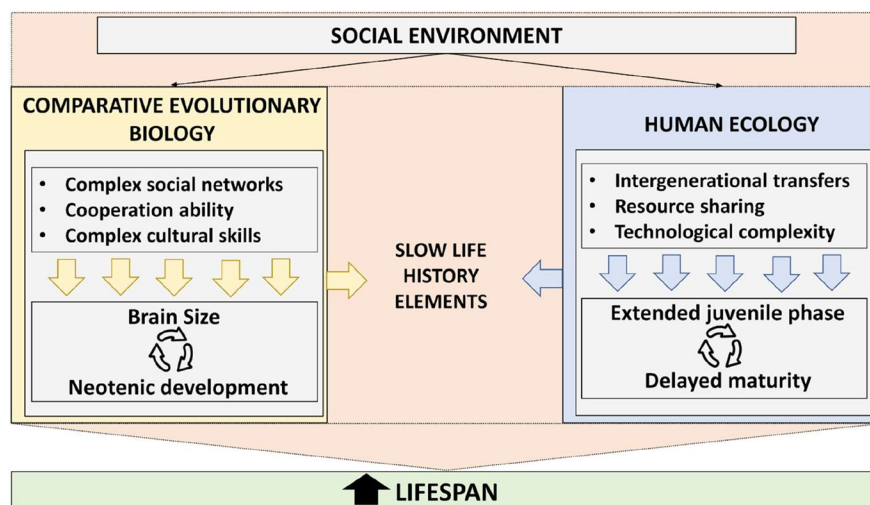
longevity and their patterns of natural variations is essential to unveil the multiple dimensions of the contemporary ageing society and to address the ongoing demographic shift.

In this chapter, we first summarize data showing how evolutionary-conserved social dynamics, such as cooperation ability in complex social interactions, contributed to the extension of the lifespan in humans with respect to other primates (section “[Insights from comparative evolutionary biology](#)” and Fig. 2 left). We then offer a brief overview on how such evolutionary-conserved dynamics are embedded in other social animal. Next, through studies in human ecology and biodemography, we point how sociality contributes to natural variation in lifespan among pre-industrial human groups, making abstraction of the confounding factors present in post-industrialized populations (such as medical practices). In particular, we will discuss how slow life history elements (such as the extended lifespan) are influenced by intergenerational transfers and resource sharing in ecological niches with higher technological complexity (see section “[Insights from human ecology and pre-industrial societies](#)” and Fig. 2 right). In conclusion, we will describe the link between sociality and natural variations in lifespan in post-industrial society (section “[Insight from post-industrial societies](#)”).

## Insights from comparative evolutionary biology

In humans, technical progress leads to an increase in life expectancy and a substantial decrease in mortality rates, especially in comparison to wild chimpanzees [66]. In fact, although the time required for the mortality rate to double is quite similar between modern human hunter-gatherers and chimpanzees [67], the percentage of surviving individuals at adult ages is much greater in the former, with an additional lifespan at age 45 about three times higher in human hunter-gatherers than in chimpanzees [68].

These observation has been explained by the fact that neoteny, marked in humans by immaturity at birth and slow postnatal maturation, extends lifespan [69]. It is hypothesized that the evolution of neoteny and longer developmental period (that in turn contribute to a longer lifespan) plays a role in brain size, structure, and connectivity typical of *Homo sapiens*. Some authors linked these changes to the specific social environment of *Homo sapiens*, for example human ontogeny occurs within the context of a highly cooperative social group whose members collaborate and interact [70]. The comparison between humans and great apes showed that human children learn more information and



**Fig. 2** Link between social environment and extended lifespan in pre-industrial society. The lens of comparative evolutionary biology provides evidences of the social determinants that favours biological mechanisms (in particular the evolution of neoteny and larger brains) responsible for the differences in extended lifespan between modern human hunter-gatherers and

other primates. The lens of the human ecology provides evidences of the social determinants that favours biological mechanisms (in particular the delayed maturity and the extended juvenile phase) responsible for the differences observed among human groups living in different ecological niches

cultural skills via teaching from others; this has been observed in societies of all types [71]. Moreover, human cultural organization in all societies is characterized by shared information between generations leading to cumulate cultural artefacts, skills, and technological knowledge.

A recent paper of Richerson and Boyd [72] presents important insights on this topic, providing evidence showing that the long, slow human life history coevolved with our large brain. Brain growth is closely linked to the high complexity of human social networks that in turn are crucial for the transmission of cultural knowledge. In this regard, it is suggested that by the late Pleistocene the diffusion of the hunting/extractive niche led to selection for larger brains and to the need for cooperative breeding to provision such brains. Thus, humans became highly dependent on complex cultural skills for subsistence and on rules to organize a complex social life. The dependency from cultural traditions and complex social networks transformed human life history elements, leading to an extended juvenile period (to learn subsistence and social skills), post-reproductive survival (to help conserve and transmit skills), and in turn, to an extended lifespan. Bioarchaeology seems to converge on similar findings: a dramatic increase in the number of adult individuals in anatomically modern humans was observed in the Early Upper Paleolithic, a process that has been linked to population expansion and cultural innovations of that period [73], likely placing the relation between social factors and human ageing way back in time. Molecular data support that the evolution of neoteny would be responsible for the difference observed in the extension of lifespan between chimpanzees and individuals of pre-industrial societies [74, 75]. The vast majority of miRNA and gene expression changes in the prefrontal cortex of humans and rhesus macaques over the species' lifespan represent reversals, or extensions, of developmental patterns [76], suggesting a link between developmental regulation and expression changes during ageing.

#### *Comparative insights from other social animals*

The naked mole rat (*Heterocephalus glaber*) offers an intriguing example of how sociality may contribute to exceptional longevity in different species. These

small, burrowing rodents are eusocial, living in large colonies with a complex social structure similar to that of some insect species, such as ants and bees [77, 78]. The colonies are typically comprised of a single breeding female, the queen, a few breeding males, and numerous non-reproductive workers. Naked mole rats are remarkable for their longevity, with lifespans that can exceed 30 years—far longer than other rodents of similar size [79, 80]. This extended lifespan is associated with several unique physiological traits, many of which are believed to be influenced by their social structure [69, 79]. The eusocial structure of naked mole rat colonies ensures a division of labour that promotes colony efficiency and survival. Non-reproductive workers undertake various tasks, including foraging and caring for the queen's offspring, which enhances the overall fitness and longevity of the colony [69, 81]. The social hierarchy and interactions within the colony may influence hormonal pathways that contribute to longevity [82]. For example, the queen's presence can affect the physiology and behaviour of other colony members, potentially enhancing their stress resistance and health [81].

Interestingly, the social hierarchy within naked mole rat colonies also introduces complexities in how stress impacts longevity [80, 83, 84]. Previous studies suggest that while the queen experiences reduced stress, subordinate individuals often face social stress due to frequent bullying [84]. This raises the question of whether subordinates, who endure chronic stress, experience reduced lifespans. Incorporating this perspective adds nuance to the understanding of how social structures, stress, and longevity interact.

The interaction between social structure and biological resilience in naked mole rats can be further understood through the lens of the exposome and allostatic load (see section “[Exposome and allostatic load](#)” for details) [63]. In naked mole rats, social cohesion and division of labour reduce allostatic load, thereby mitigating chronic stress and its detrimental effects on health [63, 64]. This reduction in allostatic load through social structures is complemented by underlying molecular mechanisms that further enhance the naked mole rat's resilience to ageing. At the molecular level, naked mole rats exhibit elevated activity of the Nrf2 gene, which regulates cellular defences against oxidative stress and inflammation, contributing to their resistance to age-related diseases such as cancer and cardiovascular conditions [63].



Further strengthening the case for the unique sociality of naked mole rats, previous studies on the vocal communication (“language”) in these animals show how their advanced social interactions may also contribute to their longevity [85]. Additionally, recent findings on prolonged pedomorphosis in naked mole rats, manifesting in sustained neurogenesis and parasympathetic-driven cardiac function, provide further evidence of the physiological benefits conferred by their eusocial structures [86].

Comparative insights from other social animals, such as elephants and dolphins, further illustrate how social structures and behaviours contribute to extended lifespans [87]. Elephants, for instance, live in matriarchal societies where older females play crucial roles in guiding and protecting the herd [87]. The matriarchs’ extensive knowledge of their environment, such as the locations of water sources and safe migratory routes, is vital for the survival of the group. Their social bonds and cooperative behaviour, including alloparental care where individuals assist in the care of offspring that are not their own, contribute to the overall health and longevity of the herd. Dolphins also demonstrate the benefits of complex social structures [88]. They live in fluid, multi-level societies where cooperation, social learning, and strong social bonds are common [88]. Dolphins engage in cooperative hunting, share knowledge about feeding strategies, and provide care for sick or injured members [88]. These behaviours not only enhance individual survival but also improve the group’s overall resilience and adaptability, leading to longer lifespans. These examples from elephants and dolphins, alongside the naked mole rat, highlight common evolutionary strategies where sociality and cooperative behaviours play pivotal roles in promoting longevity. In all these species, social structures facilitate resource sharing, collective defence against predators, and efficient care for the young and vulnerable, thereby enhancing survival rates and extending lifespans. These insights underscore the potential for sociality to drive longevity across diverse taxa, offering a broader understanding of the interplay between social behaviour and ageing. By examining these diverse species, we can better understand the evolutionary advantages of sociality and its impact on lifespan. The mechanisms observed in naked mole rats, elephants, and dolphins provide valuable models for exploring how social structures and behaviours may

influence human ageing and longevity, emphasizing the importance of fostering social connections and support networks in promoting healthy ageing.

While many social species display exceptional longevity, there are notable exceptions that challenge the straightforward correlation between sociality and lifespan. For instance, antelope species, which live in herds, have relatively short lifespans despite their social organization [89]. Similarly, solitary species like the *Spalacidae* mole rats exhibit remarkable longevity despite their lack of complex social structures [89]. These examples highlight that factors such as predator pressure, metabolic demands, and ecological niches may play crucial roles in determining lifespan, independent of social behaviours. This suggests that while sociality is a significant factor, it is not the sole determinant of longevity and must be considered alongside other evolutionary and ecological pressures.

#### Insights from human ecology and pre-industrial societies

Studies in human ecology and observations of pre-industrial societies provide evidence about the role of sociality, in the form of intergenerational transfers of food, knowledge, and skills, on certain life-history traits, such as delayed maturity, extended juvenile phase, and in turn extended lifespan [40, 56, 90, 91]. However, how the social environment shapes human lifespan extension depends mainly on the technical complexity of a given niche, related in particular to the required skills and knowledge (such as the hunting method or the foraging complexity). In fact, according to [74], technical progress may be responsible for the great differences in the mortality risks of individuals living in different ecologies. Recently, the role of intergenerational transfers in shaping extended lifespan in high-skill foraging niches has been described considering eight different populations of contemporary human hunter-gatherers and horticulturalists [92]. The authors used a demographic approach and combining data on the caloric production and demand with survival and fertility data. They noted that skills-intensive foraging ecology, where late adult independence and late peak production are observed, select for certain slower human life-history traits through positive feedback between longevity and late-life transfers. In particular, they showed that

intergenerational transfers of production surpluses from adults to juveniles favour the extension of the learning phase and the delayed maturity [92]. These observations were recently supported by another study on 714 children and adolescents from 28 pre-industrial societies [93]. This study showed that foraging returns increase slowly in skills-intensive foraging ecological niches, where resources (tubers and game) are more difficult to extract, and thus the peak production is observed late in adulthood. On the other hand, foraging returns increase rapidly during childhood for easier-to-extract resources (fruit and fish/shellfish), and thus the peak of productivity is reached by adolescence [93]. Since the lower productivity during the learning phase is offset by a higher productivity at adult ages, the time spent in the acquisition of high-level skills and knowledge drives the selection of lower adult mortality rates and extended lifespan, because the return on investment in learning occurs at older ages, when the productivity is higher [55, 92].

The study of family structure and features in different human populations is also crucial for understanding the complex relation between sociality and ageing and influence intergenerational transfer. For example, family structures in pre-industrial societies play a pivotal role in shaping intergenerational transfers and supporting sociality. Extended kin networks, including grandparents and other relatives, provide essential support in child-rearing and resource sharing [94]. These kin networks not only enhance survival rates by pooling resources but also foster pro-social behaviour and cultural transmission among family members, contributing to the overall health and longevity of the community.

Thus, the intricate interplay of family structure, social dynamics, and resource sharing highlights the critical role that sociality plays in shaping health and longevity outcomes in traditional societies.

#### Insight from post-industrial societies

In post-industrial societies, the concept of “intergenerational transfers” is much more complex because it is not limited only to the transfers of food, knowledge, and skills that we observe in pre-industrial societies, but it includes also different kind of transfers, such as those that involve public programmes at different life-cycle stages, as well as all private familial

transfers. Nevertheless, it is well established that prosocial behaviour and social integration have been positively associated with health and reduced mortality in many post-industrial societies [3, 95]. In the last decades, death rates of aged populations have sharply declined thanks to a well-developed medical system [96], but most probably, thanks also to factors including, between many others, the level of social support present in these societies [97].

The notion that the level and the quality of social support have a direct effect on health and mortality became popular thanks to two ground-breaking reviews published in 1976 [98, 99]. Both studies argued that social support, particularly from closely related individuals, could protect from the physiological and psychological consequences of exposure to stressful situations improving the resistance to pathogens or other health menaces. In 1979, a study performed on a random cohort of about 7000 adults from Alameda County (CA, USA) which were followed for at least 9 years demonstrated that individuals with higher social and community relations have a lower probability of death than those with few social interactions, independently from other lifestyle or medical factors [100].

A plethora of studies and meta-analyses, summarized by Jaime Vila in 2021 [97], have provided experimental ground for the role of social relations and intergenerational transfers in determining the health status and longevity of individuals in an industrial society.

Recently, a study on 34 post-industrialized countries, using the data from NTA project (<https://ntaccountries.org/>), demonstrated that these transfers (both within families and within communities) are negatively related to national mortality and positively related to longevity, suggesting (1) a beneficial effect of pro-social behaviour on population longevity [11] and (2) that this effect is present at different life stages [101].

Cultural differences and variations in family structure across human populations significantly influence the relationship between sociality and longevity. A clear example of that is seen in the Chinese social norm of preference for sons. In China, the cultural preference for sons profoundly shapes the social support structures available to older adults, particularly in rural areas where traditional patriarchal and patrilineal norms remain influential. Recent research

highlights that rural women who live with their sons benefit from stronger support networks, especially from non-relative friends [102]. This support is significantly enhanced by the presence of sons, as they are culturally seen as the primary caregivers and providers of old-age security. In contrast, this pattern does not extend to rural women living with daughters, reflecting the deep-rooted cultural expectations that prioritize sons in the provision of care and social resources. Such findings underscore the gendered nature of support systems in rural Chinese communities, where sons, more than daughters, facilitate broader social engagement and contribute to the well-being and ageing process of older adults [102].

Similarly, the ways in which cultural norms shape intergenerational support and social interactions vary significantly across different cultural contexts. For instance, in many Asian cultures, the expectation of filial piety drives children to provide both financial and emotional support to their ageing parents. This expectation reinforces family ties favouring care practices that significantly enhance the well-being of older adults and foster longevity [103]. In contrast, Northern European societies, where comprehensive welfare systems provide substantial support for the elderly, exhibit different patterns of intergenerational transfers [104]. However, while these societies demonstrate lower rates of upward financial transfers from children to parents, the emotional support provided by family remains crucial for mental health and resilience for the elderly [105, 106]. Southern European countries often maintain strong family cohesion, where intergenerational transfers are characterized by frequent support from adult children to their parents. This cultural emphasis on familial obligations fosters close-knit relationships, enhancing both social support and health outcomes for older adults. In these societies, grandparents are often actively involved in childcare, contributing to a robust intergenerational exchange that benefits the family unit as a whole [105, 106].

The sum of these findings confirms a direct correlation between the degree of social interactions and reduced risk of disease and mortality, where resource sharing and intergenerational transfers play a major role. Furthermore, the interplay of family structure, kinship ties, and social support is essential for understanding how sociality contributes to health outcomes in post-industrial societies.

### *Blue Zones: socio-cultural determinants of longevity*

“Blue Zones” are regions around the world identified as having populations with significantly higher-than-average lifespans [107–109]. Blue Zones include five key regions: Okinawa (Japan), Sardinia (Italy), Nicoya Peninsula (Costa Rica), Ikaria (Greece), and the Seventh-day Adventist community in Loma Linda (CA, USA) [109]. These areas share unique socio-cultural and environmental traits that contribute to their inhabitants’ exceptional longevity [109]. Individuals living in Blue Zones have been observed to exhibit a biological age younger than their chronological age [110]. This region-specific deceleration of ageing processes in inhabitants of Blue Zones and other similar longevity regions is attributed to the distinctive lifestyle and social factors deeply embedded in their cultures, which promote both physical and social health [109, 111, 112]. These practices include strong social networks.

In Blue Zones, maintaining close-knit communities and strong family ties is a fundamental aspect of daily life [111, 113–116]. For instance, Okinawans practice “moai”, a tradition of forming lifelong social networks that provide financial and emotional support [117]. Similarly, Sardinians maintain robust familial bonds and social cohesion, which fosters a sense of belonging and security [118]. Many Blue Zone cultures emphasize the importance of intergenerational living, where multiple generations reside together or in close proximity [109, 118]. This living arrangement promotes the exchange of knowledge, wisdom, and care across generations, enhancing the well-being of both younger and older members. When elder family members play active roles in the upbringing of children, it reinforces family bonds and provides a sense of purpose for the elderly. Strong social networks play a crucial role in cultivating a sense of purpose, a key insight from Blue Zones research. In regions like Okinawa and Nicoya, this sense of purpose is known as “ikigai” [119, 120] and “plan de vida” [109], respectively. A well-defined purpose in life greatly enhances psychological resilience and competence, promoting motivation, determination, and a positive outlook [121]. These robust social networks provide emotional support, social engagement, and opportunities for meaningful roles within the community, enhancing individuals’ feelings of connectedness and belonging. This interconnectedness

helps to reduce stress and anxiety, protecting against the harmful effects of chronic stress on biological ageing processes [122, 123].

The social structures and cultural practices in Blue Zones exemplify the positive impact of sociality on ageing and longevity. The strong social networks, intergenerational interactions, and communal support systems provide emotional stability, reduce stress, and promote mental health. These social factors are crucial in mitigating the detrimental effects of social isolation and loneliness, which are significant risk factors for morbidity and mortality in ageing populations. Understanding the socio-cultural and environmental factors that contribute to the longevity of Blue Zone populations offers valuable insights for ageing societies worldwide. Promoting social connections, fostering intergenerational relationships, encouraging activities that result in stress reduction can collectively enhance the healthspan and lifespan of individuals. The integration of these principles into public health policies and community planning can help address the challenges of an ageing population, fostering environments that support longevity and well-being.

The fact that supportive social relationships are important for well-being and longevity suggests that understanding the neurological and biological factors underlying this phenomenon could pave new avenues to improve quality and duration of life [124].

### Physiological mechanisms linking sociality and lifespan

As mentioned above, the impact of social environment on health and lifespan is a conserved feature of human populations, and several mammalian orders [10, 34] suggesting the involvement of shared evolutionary-conserved physiological processes (Fig. 3). The social environment has been identified both as a source of relief and one of the primary sources of challenging stimuli that can induce a stress response [125]. “Stress” is the process through which an organism reacts to environmental stimuli that challenge the stability of either its physiological conditions (homeostasis) or of its mental/psychological landscape, whereas “stress response” is the activation of key physiological or neuropsychological pathways aimed to maintain organism stability and survival in a challenging environmental context.

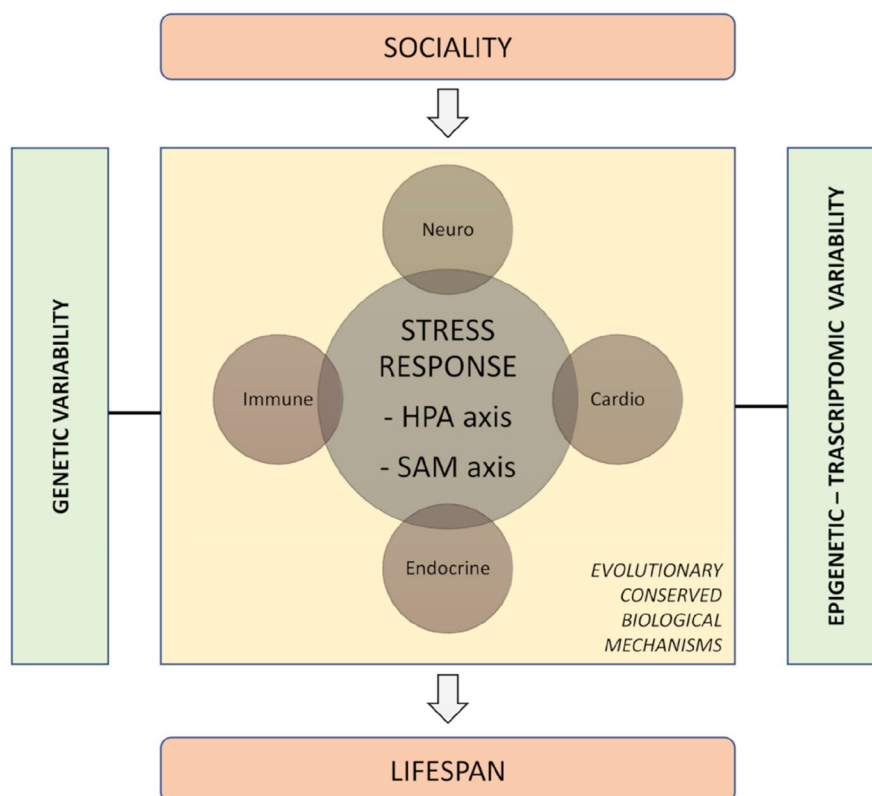
Chronic socially induced stress exposure in humans and animal models accelerates the progression of metabolic, cardiovascular, and neurological diseases as well as malignancies [126] and is a predictor of several mental and physical health conditions including depression, schizophrenia, bipolar disorder, cardiovascular disease, autoimmune disorders, and impaired cognitive functions [127–134]. More generally, chronic stress is associated to earlier mortality [135], and experimental animal models exposed to stress present a shortened lifespan that can be alleviated by social interactions: according to the so-called stress-buffering hypothesis, “the availability of a conspecific reduces the activity of stress-mediating neurobiological systems” [136].

### Neurophysiological pathways of stress

The neurophysiological pathways involved in the activation of the response to stress implicate the hypothalamus and other brainstem areas involved in inducing specific defensive reactions (freezing, startle response, fight-or-flight) through activation of the autonomic nervous system and of the neuroendocrine system. It has been suggested that the chronic activation of these defensive pathways, also called the “default stress response” [137, 138], transforms their physiological effects from life-saving to self-harming favouring increase morbidity and mortality through deregulation of the cardiovascular, neuroendocrine, and immune systems.

Two neurophysiological signalling systems are involved in the activation of a stress response: the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic-adrenomedullary (SAM) system. Their activation results in the increases of circulating glucocorticoids (cortisol) and catecholamines (adrenaline) respectively which, both, are needed to prepare the body for a fight-or-flight response. An initial threatening sensory input activates cerebral cortical and subcortical structures including the amygdala and the hypothalamus, and finally induces autonomic, endocrine, and motor responses to protect the organism from the menace. The “stress-buffering hypothesis” suggests that social support has positive effects on health status and longevity through the reduction of the negative effects that prolonged activation of the HPA and SAM axes has on different physiological systems.

**Fig. 3** Social dynamics impacts on evolutionary conserved mechanisms of stress response that involved HPA (hypothalamic–pituitary–adrenal) and SAM (sympathetic–adrenomedullary) axes. The effect of sociality—in reason of the systemic nature of stress response—has been observed in immune, neuroendocrine, and cardiovascular systems. These biological changes that could include both genetic and epigenetic changes can ultimately influence lifespan



Interestingly, both these systems converge on the adrenal gland, which has been implicated in another important theory of sociability: the domestication syndrome. Seminal observations have proposed that the selection of breeders from generation to generation on the sole criterium of “docility”, an adrenal phenotype, induced the co-selection of hormonal, behavioural, and anatomical traits [139, 140]. In humans, some theories propose that an auto-domestication occurred during human evolution [141–143], favouring individuals with higher sociability.

Furthermore, experimental studies in humans have confirmed the importance of the HPA axis for the stress-buffering effect exerted by positive social input: indeed, exposure to attachment figures provokes cortisol level reduction at different periods of life [136, 144]. The involvement of the SAM signalling system on stress-buffering has been more difficult to demonstrate experimentally due in great part to methodological difficulties [97, 145, 146].

The link between socially induced stress and physiological mechanisms involved in different life-history traits has been demonstrated also in non-human

experimental studies, suggesting that crucial biological mechanisms are involved. A study on red squirrels [147] showed that social “negative” cues have an intergenerational effect on the growth rate, and more precisely, that high-density cues, accomplished via playbacks of territorial vocalizations, led to increased offspring growth rates. A higher social-induced stress would increase glucocorticoid levels in mothers, which in turn affect the growth rate of the pups. However, offspring born from social stressed mothers have a reduced adult lifespan [148], suggesting that faster offspring growth might incur a cost to offspring later in life. Thus, these studies suggest an indirect link between sociality and lifespan, mediated by physiological and behavioural stress response of mothers and the resulting consequences on the offspring.

Effects of social isolation and stress on the cardiovascular system

In his famous lecture at the Sorbonne in 1885, Claude Bernard discussed how the physiology of the heart was intimately connected to that of the brain and

how cardiac activity was in part mediated through the vagus nerve [149]. Indeed, heart rate is regulated by the autonomic sympathetic and parasympathetic nervous systems [150]: the sympathetic nervous system increases heart rate, whereas the parasympathetic nervous system reduces it.

Prolonged stress results in imbalanced regulation of the heart with increased sympathetic and decreased parasympathetic stimulation, resulting in higher heart rate with increased morbidity and mortality [138]. A reciprocal interconnection between the brain and the heart is at the origin of the integration of cognitive, affective, and autonomic systems in a dynamic model of stress regulation suggesting that reduced stress would stimulate the prevalence of the parasympathetic system resulting in increased health and longevity [151, 152]. In a safe milieu and in a socially supportive situation, an increased parasympathetic control by the vagus nerve would slow the heart, reduce the activity of the HPA axis, and avoid fight-flight sympathetic response.

A recent study [153] has determined a direct association between social isolation, loneliness, and coronary heart disease and stroke mortality. According to this study, social isolation and loneliness are associated with about a 30% increased risk of heart attack or stroke, or death from either. Evidence is most compelling for an association between social isolation and death from heart disease and stroke, with a 29% increase in the risk of heart disease death, and a 32% increased risk of stroke and stroke death [154]. It seems plausible that chronic physiological and psychological responses to social isolation-stress might be at the origin of this increased risk of death suggesting that measures are taken to alleviate social isolation in our society.

#### Endocrine effects on sociality and ageing

During ageing, the endocrine system becomes less efficient, resulting in a parallel decline of social and physiological capacities with increased morbidity and a higher risk of death. For example, in men, low testosterone levels lead to a progressive decline in muscle and bone mass with reduced physical performances and, in women, loss of oestrogens strongly increases the risk of osteoporosis and fracture.

The main hormones involved in the control of social behaviour are the two nonapeptides

oxytocin (OT) and arginine-vasopressin (AVP), and the gonadal hormones testosterone and oestrogens. These hormones mutually regulate their secretion and converge on the regulation of target organs through complex interacting pathways. OT and AVP are among the earliest neurohormones appeared during evolution [155], they are produced by magnocellular neurons in the hypothalamus and are then secreted in the blood stream and act throughout the brain [156, 157]. Centrally, these hormones target brain regions involved in social cognition including the amygdala, the striatum, and the hippocampus [158].

OT is a neuropeptide produced by the paraventricular nucleus of the hypothalamus and released into the circulation by the posterior pituitary. OT release in the brain is involved in the formation of mother-offspring bonds [159]. It is also involved in the regulation of the HPA axis, both in response to a stressing situation or to the presence of social support [160, 161], resulting in the activation of pro-social protective behaviours.

AVP has a chemical structure closely related to that of OT [162]. Besides its fundamental physiological functions in the control of blood pressure and kidney function, AVP has been shown to play an important role in determining the social behaviour of many vertebrate species [163–168].

In mammals, AVP is produced by several hypothalamic regions including the paraventricular (PVN), supraoptic (SON), supra-chiasmatic nuclei (SCN), the nucleus circularis (NC), and the preoptic area (POA). Furthermore, AVP is produced by specific sensory regions of the CNS including the olfactory bulb (OB) and by the amygdala where its expression is steroid-dependent and sex-specific [169]. The effects of AVP and OT on social behaviours are due to their ability to activate brain regions involved in social recognition [170], maternal care, pair bonding, communication [171], aggression, cognition [172], and stress and anxiety-like behaviours [173, 174].

Various studies have shown that OT, AVP, and gonadal hormones interact to determine social recognition and social behaviours [175]. For example, oestrogen enables social recognition by regulating hypothalamic OT production and its receptors in the medial amygdala. In male rodents, AVP stimulates social recognition by acting on the lateral septum. In general, it appears that the fine regulation exerted by gonadal hormones on OT and AVP can adjust social

behaviours in a sex-specific manner, reinforcing the notion of the central role of these neuroendocrine systems in the regulation of the sex-specific behaviours. These behavioural effects do not only impinge on reproduction, but affect more globally the insertion of individuals in a social structure. During ageing, the progressive reduction of gonadal hormones both in males and females reorients social behavioural patterns, adapting them to the different epochs of life.

#### Immunity and inflammation and the relation between sociality and lifespan

The major role of the immune system is to protect the organism from external pathogens through the process known as inflammation. The inflammatory reaction is activated by small secreted proteins known as pro-inflammatory cytokines which include, for example, IL-1, IL-6, and TNF- $\alpha$ . These cytokines are released predominantly by Th1 cells, CD4+ cells, macrophages, and dendritic cells. They play a central role in regulating proliferation, activation, differentiation, and homing of immune cells to the sites of infection where they can fight pathogens, including viruses (see, for example [176]). In addition to immune cells, several other organs and tissues also release inflammatory cytokines. Adipocytes can secrete pro-inflammatory cytokines such as IL-6 and TNF- $\alpha$ , especially in the context of obesity [129, 177–181]. This chronic low-grade inflammation in adipose tissue is a significant contributor to metabolic disorders and age-related heightened state of systemic inflammation. Endothelial cells lining the blood vessels can also produce cytokines like IL-1 and IL-6 [182]. Age-related endothelial inflammation plays a key role in the development of atherosclerosis and other cardiovascular diseases as well as vascular cognitive impairment and neurodegenerative diseases [183, 184].

Beside their action on the immune system, pro-inflammatory cytokines also affect the activity of the brain and can influence social behaviour increasing sensitivity to both negative and positive social experiences, which results in variations of the likelihood to develop diseases or face pathogens [185, 186]. Furthermore, negative social experiences such as parental separation, mourning, isolation, and loneliness influence directly the immune system by increasing pro-inflammatory cytokines [187]. A large meta-analysis,

based on 41 independent studies, confirmed these findings showing a significant correlation between low social support and inflammation [188]. Chronic inflammation associated with low social integration and/or social support can affect negatively the risk of many common pathologies including cancer, diabetes, cardiovascular disease, kidney disease, neurodegenerative disorders, non-alcoholic liver disease, and autoimmune diseases, causing higher morbidity and mortality [189].

Moreover, Yang and colleagues [101] provided evidence on the role of social connections on reducing the risk of inflammation and hypertension in adolescence, young, and late adulthood, suggesting that the impacts of social relationships on physiological mechanisms emerge in adolescence and midlife, but persist also into old age. From this point of view, the impact of sociality on inflammation could be seen as an effect on the rate of ageing, contributing to the process known as “inflammageing” [13]: the sterile, low-grade inflammation that develops while growing older and contributes to the pathogenesis of age-related diseases. The process of inflammaging is driven by multiple factors, including the accumulation of senescent cells, which secrete pro-inflammatory cytokines, chemokines, and other factors collectively known as the senescence-associated secretory phenotype (SASP) [190, 191]. These secreted factors contribute to chronic, low-grade inflammation and can affect the surrounding tissue environment. Chronic inflammation from SASP can exacerbate tissue damage and contribute to the development of age-related diseases. Inflammaging is characterized by an increase in circulating pro-inflammatory cytokines and is associated with a higher risk of many age-related diseases, such as cardiovascular disease, type 2 diabetes, neurodegenerative diseases, and certain cancers. This chronic inflammatory state stimulates the senescence of the immune system reducing its capacity to eliminate senescent cells and inflammatory factors, creating a self-sustaining cycle of inflammation and senescence. In this sense, inflammation has been recognized as one of the hallmarks of ageing, and its reduction could be a potential strategy for anti-ageing intervention [192]. Low social integration is, from this perspective, one of the many stimuli which contribute to the inflammaging process determining the evolution of morbidity and longevity [192, 193]. Indeed, many studies have confirmed that social

stressors are particularly strong triggers of inflammation [194–196].

It has been shown that a feedback regulatory loop exists between the function of the immune system and socio-behavioural conditions. Indeed, on one side, psychoneuroimmunology has shown that the quantity and quality of social connections can directly affect immune responses, while, on the contrary, pathological conditions can transiently affect social interactions as it has been seen, for example, during the COVID-19 pandemic. “Social immunology” is a research approach, which integrates socio-economic, political, and environmental factors with the effects of pathogen exposure on the immune responses. Social immunology is therefore a “holistic understanding of the effects of social contexts on the patterning of morbidity and mortality” highlighting risk factors related to impaired immune function [197, 198]. Understanding the complex interplay between sociality, immunity, and inflammation can inform strategies to improve health and longevity. Interventions aimed at enhancing social support and reducing social isolation could mitigate the inflammatory processes associated with ageing and chronic diseases, thereby promoting healthier ageing and extended lifespan.

### Genetic and epigenetic mechanisms linking sociality and lifespan

The association between lifespan and social behaviours has very profound roots. This observation implies the presence of significant genetic and epigenetic factors that are shaped by social dynamics and, in turn, play a role in the natural variations observed in lifespan.

Understanding these genetic and epigenetic determinants is an entry point to decipher the impact of sociality on the physiological mechanisms which determine human ageing.

#### Genetics

The fact that social behaviour in many mammalian species, including humans, is associated with lifespan suggests that some evolutionary conserved and highly pleiotropic genetic mechanisms might be involved.

An interesting example is given by the targeted inactivation of *Dlx5* and *Dlx6* which encode two homeobox transcription factors expressed by developing and mature GABAergic interneurons in the forebrain. Mice in which *Dlx5* and *Dlx6* are simultaneously inactivated selectively in GABAergic interneurons present a hyper-vocalization and hyper-socialization phenotype and behavioural patterns suggesting reduction of both anxiety-like behaviour and obsessive–compulsive activities [199]. These animals present also a 25% body weight reduction associated with a marked decline in white and brown adipose tissue. Remarkably, both inactivation of *Dlx5/6* in GABAergic neurons results in a 33% longer median survival and hallmarks of biological ageing are all improved in these mutant animals. These data imply that GABAergic interneurons can at the same time regulate social behaviour and lifespan through *Dlx5/6*-dependent mechanisms. Interestingly, comparison of the *DLX5/6* genomic regions from Neanderthal and modern humans has permitted to identify an introgressed Neanderthal haplotype (*DLX5/6*-N-Haplotype) present in 12.6% of European individuals that covers *DLX5/6* coding and regulatory sequences. The *DLX5/6*-N-Haplotype is not significantly associated to “autism spectrum disorders” but includes the binding site for GTF2I, a gene associated to Williams–Beuren syndrome, a neurodevelopmental disorder characterized by hyper-sociality and hyper-vocalization. Interestingly, the *DLX5/6*-N-Haplotype is significantly underrepresented in semi-supercenarians (> 105 years of age), a well-established human model of healthy ageing and longevity, suggesting its potential involvement in the co-evolution of longevity, sociability, and speech [200].

An experimental evidence comes from the study of Schwarz and colleagues [201] based on the genetics of neurodegenerative disease. The authors provide some evidence that alleles located in CD33 gene that protect against age-related cognitive deterioration could result from kin selection late in life through increased survival of younger kin. Extended lifespan is certainly an even more complex phenotype where neurological health is one of the most important factors. The authors support the notion that selection by inclusive fitness may be strong enough to favour alleles protecting from cognitive decline, a condition that would have compromised the emergence of cumulative culture.



## Epigenetics and gene regulation

Epigenetic changes are among the most important molecular “hallmarks of ageing” [202] and are associated to the decline in cellular functions seen in ageing and age-related conditions. During ageing, epigenetic changes can lead to aberrant gene expression, reactivation of transposable elements, and genomic instability [203]. DNA methylation (DNAm), one of the most important epigenetic modifications observed during ageing, mediates the effect of the early-social environment on later-life phenotypes [204–206]. A recent study on a wild population of spotted hyenas [207] found that more maternal care and social connectedness during the later subadult life stage, after leaving the den, are associated with higher global (%CCGG) DNAm, a marker of genomic instability and overall health. This same study has also identified differential DNAm in five genes related to inflammation, immune response, and ageing that may connect maternal care and the manifestation of stress-related phenotypes later in life.

The importance of DNAm as the process at the interface between the early social experiences and later-life phenotypes extends also to our own species. A recent study [208], using methylation data of 494 participants (age 20–22 years) recruited from a longitudinal birth cohort survey in the Philippines, showed that nutritional, microbial, and psycho-social exposures in infancy and childhood predict adult levels of DNAm in genes that shape inflammatory phenotypes implicated in cardiovascular diseases. A later study [209], using methylation data of the same cohorts, found that low socio-economic status (SES), from infancy to young adulthood, predicts the DNAm levels of 2546 CpG sites. These CpG sites were found across 1537 genes that are involve biological pathways related to immune function and development of the nervous system.

Thus, these studies suggest that early social experiences can influence DNAm of genes involved in physiological processes that contribute to the development inflammation-related diseases later in life.

## Biomarkers and future perspective

Starting from the 1980s, the necessity for valid and reliable biomarkers of ageing became evident in the pursuit of comprehending, slowing, stopping, and

potentially reversing the ageing process. Recognizing the limitations of chronological age as a flawed proxy for ageing, Baker and Sprott [210] suggested pinpointing biomarkers capable of precisely and swiftly forecasting an individual’s or an organ’s functional capability and its evolution over the life span. In essence, their proposal aimed to identify markers representing biological age rather than relying solely on chronological age [210]. Among the various measures, epigenetic clocks are the most promising biomarkers of biological ageing. Epigenetic clocks are mathematical models built on the combinations of DNAm levels of CpG sites across the genome and a significant body of literature offers compelling evidence regarding the ability of these biomarkers to encompass facets of biological ageing [211]. To date, several DNAm-based epigenetic clocks have been developed through various methods. The “first-generation” clocks (*Horvath* [212] and *Hannum* [213]) were designed to estimate chronological age; the “second-generation” clocks (*PhenoAge* [214] and *GrimAge* [215]) were specifically developed to forecast health-related outcomes and predict the time to death; whereas the third-generation epigenetic clock (*DunedinPACE* [216]) was intended to track and comprehend the impact of ageing interventions along with how changes in disease conditions or lifestyle choices influence epigenetic ageing.

Furthermore, these clocks are applicable across all types of DNA sources (ranging from sorted cells to various tissues and organs) and encompass the entire age range (from prenatal tissue development to tissues found in centenarians) [212]. In general, a positive discrepancy between biological age, as estimated by these clocks, and the chronological age, indicates that the underlying tissue/organs ages faster than expected.

Although many studies investigated the effect of early life adversity on the epigenetic clocks [217–219], how the social environment and the social interactions can impact on them is still poorly understood. One remarkable finding on this topic came from the paper of Hillman and colleagues [220]. In this study, using data from Health and Retirement Study (a nationally representative study of adults over the age of 50 and their spouses), the authors found that positive social factors slow biological ageing. Specifically, their study demonstrated that increased support from friends and more frequent contact with

friends were associated to a decelerated Pace of Ageing, as assessed by the *DunedinPACE* clock. Additionally, they observed that greater contact frequency with children correlated with a reduced *GrimAge*, and that an uptick in family contact over time was connected to a decreased *Hannum* age [220].

In addition to epigenetic clocks [221, 222], future research could explore other biomarkers that assess the impact of sociality on ageing. Potential biomarkers include inflammatory markers like C-reactive protein, interleukin-6 (IL-6), and other inflammatory cytokines, which are indicative of chronic inflammation—a condition linked to social isolation and stress [223, 224]. Telomere length, a marker of cellular ageing and biomarkers of oxidative stress, could also be evaluated in relation to social interactions, as chronic stress and isolation have been associated with telomere shortening and increased oxidative macromolecular damage [225]. Cortisol levels, reflecting stress-induced endocrine responses, can offer insights into the physiological toll of social stress across different life stages [226, 227]. Neuroimaging studies of brain regions involved in social cognition and stress regulation, such as the amygdala and prefrontal cortex, may also provide valuable insights into how social environments shape biological ageing processes [228].

As our knowledge of epigenetic clocks and other biomarkers of ageing advances, these tools offer a valuable unique opportunity to inform and guide public health and social policies aimed at promoting healthy ageing. Policymakers could harness longitudinal data on DNA methylation and other biological markers to design tailored interventions that address distinct ageing trajectories within different socio-economic and cultural groups and communities. In particular, in post-industrial societies, epigenetic clocks could serve as a critical measure to evaluate the effectiveness of social interventions guided by evidence-based policies. Furthermore, policies that provide support from prenatal stages through childhood and into old age could significantly reduce the risk of chronic diseases linked to accelerated biological ageing. Indeed, research has shown that ageing processes begin early in life, shaped by factors such as prenatal and early childhood environments. By addressing these early influences, such policies can promote healthier ageing trajectories and mitigate long-term health risks.

In this perspective, further studies aimed at exploring the influence of pro-social behaviours and social interactions on epigenetic clocks are essential. These studies can pave the way for evidence-based social policies that facilitate healthy ageing within a rapidly evolving social environment.

## Conclusions

In this review, we have summarized with a bioanthropological perspective the profound relationship between sociality and longevity. We show that social dynamics can shape various aspects of physiology, including neuronal, cardiovascular, endocrine and immune systems at the cellular and molecular levels, all converging on the mechanisms of stress response that, in turn, influence lifespan. We provide evidence on how sociality can influence biological mechanisms across different timescales, impacting, at different epochs of life, human ageing, and lifespan. We conclude that lifespan and healthy ageing result from the complex interplay between genetic/physiological determinants and socio-ecological factors at both individual and population levels. This complex regulatory network contributes, on an evolutionary timescale, to different life-history trajectories and lifespan variations. We emphasize the importance of interdisciplinary research capable of integrating all the above-mentioned dimensions with the final goal of identifying potential interventions to improve human healthy ageing in rapidly evolving social environment.

**Funding** This research was partially supported by the ANR grant METABRAIN (ANR-21-CE14-0072) to GL and the grant “Brain control of healthy ageing: implication of DLX5/6 expression in GABAergic neurons” from the “Fondation-NRJ–Institut de France” (N° 216612) given to NNN and GL. We acknowledge funding from Next Generation EU, in the context of the National Recovery and Resilience Plan, Investment PE8 – Project Age-It: “Ageing Well in an Ageing Society” [DM 1557 11.10.2022]. The views and opinions expressed are only those of the authors and do not necessarily reflect those of the European Union or the European Commission. Neither the European Union nor the European Commission can be held responsible for them. This resource was co-financed by the Next Generation EU.

## Declarations

**Competing interests** The authors declare no competing interests.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

## References

- World Health Organization. National programmes for age-friendly cities and communities: a guide. Geneva, 2023.
- Niccoli T, Partridge L. Ageing as a risk factor for disease. *Curr Biol*. 2012;22:R741–52.
- Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. Brayne C (ed.). *PLoS Med*. 2010;7:e1000316.
- Committee on the Health and Medical Dimensions of Social Isolation and Loneliness in Older Adults, Board on Health Sciences Policy, Board on Behavioral, Cognitive, and Sensory Sciences et al. Social isolation and loneliness in older adults: opportunities for the health care system. Washington, D.C.: National Academies Press, 2020:25663.
- World Health Organization. Social isolation and loneliness among older people: advocacy brief. Geneva, 2021.
- Holt-Lunstad J, Smith TB, Baker M, et al. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci*. 2015;10:227–37.
- Chin B, Murphy MLM, Cohen S. Age moderates the association between social integration and diurnal cortisol measures. *Psychoneuroendocrinology*. 2018;90:102–9.
- Ertel KA, Glymour MM, Berkman LF. Effects of social integration on preserving memory function in a nationally representative US elderly population. *Am J Public Health*. 2008;98:1215–20.
- Loucks EB, Berkman LF, Gruenewald TL, et al. Relation of social integration to inflammatory marker concentrations in men and women 70 to 79 years. *Am J Cardiol*. 2006;97:1010–6.
- Snyder-Mackler N, Burger JR, Gaydos L, et al. Social determinants of health and survival in humans and other animals. *Science*. 2020;368:eaax9553.
- Vogt T, Kluge F, Lee R. Intergenerational resource sharing and mortality in a global perspective. *Proc Natl Acad Sci*. 2020;117:22793–9.
- Medvedev ZA. An attempt at a rational classification of theories of ageing. *Biol Rev*. 1990;65:375–98.
- Franceschi C, Bonafè M, Valensin S, et al. Inflammaging: an evolutionary perspective on immunosenescence. *Ann N Y Acad Sci*. 2000;908:244–54.
- Kirkwood TBL. Evolution of ageing. *Nature*. 1977;270:301–4.
- Medawar PB. An unsolved problem of biology: an inaugural lecture delivered at University College, London, 6 December, 1951. H.K. Lewis and Company, 1952.
- Williams GC. Pleiotropy, natural selection, and the evolution of senescence. *Evolution*. 1957;11:398–411.
- Crimmins EM. Social hallmarks of aging: suggestions for geroscience research. *Ageing Res Rev*. 2020;63:101136.
- Hamilton WD. The genetical evolution of social behaviour. *I J Theor Biol*. 1964;7:1–16.
- Lehmann L, Keller L. The evolution of cooperation and altruism – a general framework and a classification of models. *J Evol Biol*. 2006;19:1365–76.
- Michod RE. The theory of kin selection. *Annu Rev Ecol Syst*. 1982;13:23–55.
- West-Eberhard M. The evolution of social behavior by kin selection. *Q Rev Biol*. 1975;50:1–33.
- Bourke AFG. Kin selection and the evolutionary theory of aging. *Annu Rev Ecol Evol Syst*. 2007;38:103–28.
- Alonso WJ, Schuck-Paim C. Sex-ratio conflicts, kin selection, and the evolution of altruism. *Proc Natl Acad Sci*. 2002;99:6843–7.
- Wilson EO, Hölldobler B. Eusociality: origin and consequences. *Proc Natl Acad Sci*. 2005;102:13367–71.
- Bourke AFG. Genetics, relatedness and social behaviour in insect societies. In: Fellowes MDE, Holloway GJ, Rolff J, editors. *Insect evolutionary ecology: proceedings of the Royal Entomological Society's 22nd Symposium*, Reading, UK, 2003. Wallingford: CABI; 2005. pp. 1–30.
- Emlen ST. An evolutionary theory of the family. *Proc Natl Acad Sci*. 1995;92:8092–9.
- Foster K, Wenseleers T, Ratnieks F. Kin selection is the key to altruism. *Trends Ecol Evol*. 2006;21:57–60.
- Trivers R. *Social evolution*. 10. [print.]. Menlo Park, Calif.: Benjamin/Cummings Publ, 1993.
- Crozier RH, Pamilo P. *Evolution of social insect colonies: sex allocation and kin selection*. Repr. Oxford: Oxford Univ. Press, 2003.
- Bourke AFG. *Principles of social evolution*. Oxford University Press, 2011.
- Queller DC, Strassmann JE. Kin selection and social insects. *Bioscience*. 1998;48:165–75.
- Negroni MA, Macit MN, Stoldt M, et al. Molecular regulation of lifespan extension in fertile ant workers. *Philos Trans R Soc B Biol Sci*. 2021;376:20190736.
- Warner MR, Mikheyev AS, Linksvayer TA. Genomic signature of kin selection in an ant with obligately sterile workers. *Mol Biol Evol*. 2017;34:1780–7.
- Zhu P, Liu W, Zhang X, et al. Correlated evolution of social organization and lifespan in mammals. *Nat Commun*. 2023;14:372.
- Archie EA, Tung J, Clark M, et al. Social affiliation matters: both same-sex and opposite-sex relationships predict survival in wild female baboons. *Proc R Soc B Biol Sci*. 2014;281:20141261.

36. Ellis S, Snyder-Mackler N, Ruiz-Lambides A, et al. Deconstructing sociality: the types of social connections that predict longevity in a group-living primate. *Proc R Soc B Biol Sci.* 2019;286:20191991.
37. Silk JB, Beehner JC, Bergman TJ, et al. The benefits of social capital: close social bonds among female baboons enhance offspring survival. *Proc R Soc B Biol Sci.* 2009;276:3099–104.
38. Hamilton WD. The moulding of senescence by natural selection. *J Theor Biol.* 1966;12:12–45.
39. Lee RD. Rethinking the evolutionary theory of aging: transfers, not births, shape senescence in social species. *Proc Natl Acad Sci.* 2003;100:9637–42.
40. Hawkes K, O'Connell JF, Jones NGB, et al. Grandmothering, menopause, and the evolution of human life histories. *Proc Natl Acad Sci.* 1998;95:1336–9.
41. Cant MA, Johnstone RA. Reproductive conflict and the separation of reproductive generations in humans. *Proc Natl Acad Sci.* 2008;105:5332–6.
42. Hawkes K, O'Connell JF, Blurton Jones NG. Hadza women's time allocation, offspring provisioning, and the evolution of long postmenopausal life spans. *Curr Anthropol.* 1997;38:551–77.
43. Hawkes K, Smith KR. Brief communication: Evaluating grandmother effects. *Am J Phys Anthropol.* 2009;140:173–6.
44. Madrigal L, Meléndez-Obando M. Grandmothers' longevity negatively affects daughters' fertility. *Am J Phys Anthropol.* 2008;136:223–9.
45. Korb J, Heinze J. Ageing and sociality: why, when and how does sociality change ageing patterns? *Philos Trans R Soc B Biol Sci.* 2021;376:20190727.
46. Kirkwood TBL. The disposable soma theory: origins and evolution. In: Shefferson RP, Jones OR, Salguero-Gómez R, editors. *The evolution of senescence in the tree of life.* 1st ed. Cambridge University Press; 2017. p. 23–39.
47. MacArthur RH, Wilson EO. An equilibrium theory of insular zoogeography. *Evolution.* 1963;17:373–87.
48. Pianka ER. On r- and K-selection. *Am Nat.* 1970;104:592–7.
49. Stearns SC. The evolution of life history traits: a critique of the theory and a review of the data. *Annu Rev Ecol Syst.* 1977;8:145–71.
50. Salinari G, De Santis G, Zarulli V, et al. Fertility decline and the emergence of excess female survival in post-reproductive ages in Italy. *Genus.* 2022;78:19.
51. Gintis H. Gene–culture coevolution and the nature of human sociality. *Philos Trans R Soc B Biol Sci.* 2011;366:878–88.
52. Carey JR, Judge DS. Life span extension in humans is self-reinforcing: a general theory of longevity. *Popul Dev Rev.* 2001;27:411–36.
53. Markov AV, Markov MA. Coevolution of brain, culture, and lifespan: insights from computer simulations. *Biochem Mosc.* 2021;86:1503–25.
54. Street SE, Navarrete AF, Reader SM, et al. Coevolution of cultural intelligence, extended life history, sociality, and brain size in primates. *Proc Natl Acad Sci.* 2017;114:7908–14.
55. Gurven M, Kaplan H. Determinants of time allocation across the lifespan: a theoretical model and an application to the Machiguenga and Piro of Peru. *Hum Nat.* 2006;17:1–49.
56. Kaplan H, Hill K, Lancaster J, et al. A theory of human life history evolution: diet, intelligence, and longevity. *Evol Anthropol Issues News Rev.* 2000;9:156–85.
57. Kaplan HS, Robson AJ. The emergence of humans: the coevolution of intelligence and longevity with intergenerational transfers. *Proc Natl Acad Sci.* 2002;99:10221–6.
58. Kaplan H, Lancaster J, Robson A. Embodied capital and the evolutionary economics of the human life span. *Popul Dev Rev.* 2003;29(1):113–20. <https://doi.org/10.1111/j.1728-4457.2003.00113.x>.
59. Milton K. A hypothesis to explain the role of meat-eating in human evolution. *Evol Anthropol Issues News Rev.* 1999;8:11–21.
60. Laden G, Wrangham R. The rise of the hominids as an adaptive shift in fallback foods: plant underground storage organs (USOs) and australopith origins. *J Hum Evol.* 2005;49:482–98.
61. Crittenden AN, Conklin-Brittain NL, Zes DA, et al. Juvenile foraging among the Hadza: implications for human life history. *Evol Hum Behav.* 2013;34:299–304.
62. Kramer KL, Ellison PT. Pooled energy budgets: resituating human energy -allocation trade-offs. *Evol Anthropol Issues News Rev.* 2010;19:136–47.
63. Shiels PG, Painer J, Natterson-Horowitz B, et al. Manipulating the exposome to enable better ageing. *Biochem J.* 2021;478:2889–98.
64. Shiels PG, Buchanan S, Selman C, et al. Allostatic load and ageing: linking the microbiome and nutrition with age-related health. *Biochem Soc Trans.* 2019;47:1165–72.
65. Stenvinkel P, Shiels PG. Long-lived animals with negligible senescence: clues for ageing research. *Biochem Soc Trans.* 2019;47:1157–64.
66. Burger O, Baudisch A, Vaupel JW. Human mortality improvement in evolutionary context. *Proc Natl Acad Sci.* 2012;109:18210–4.
67. Finch CE, Pike MC, Witten M. Slow mortality rate accelerations during aging in some animals approximate that of humans. *Science.* 1990;249:902–5.
68. Hill K, Boesch C, Goodall J, et al. Mortality rates among wild chimpanzees. *J Hum Evol.* 2001;40:437–50.
69. Skulachev VP, Holtze S, Vysokikh MY, et al. Neoteny, prolongation of youth: from naked mole rats to “naked apes” (humans). *Physiol Rev.* 2017;97:699–720.
70. Tomasello M. The adaptive origins of uniquely human sociality. *Philos Trans R Soc B Biol Sci.* 2020;375:20190493.
71. Hewlett BS, Roulette CJ. Teaching in hunter–gatherer infancy. *R Soc Open Sci.* 2016;3:150403.
72. Richerson PJ, Boyd R. The human life history is adapted to exploit the adaptive advantages of culture. *Philos Trans R Soc B Biol Sci.* 2020;375:20190498.
73. Caspari R, Lee S-H. Older age becomes common late in human evolution. *Proc Natl Acad Sci.* 2004;101:10895–900.
74. Skulachev VP, Shilovsky GA, Putyatina TS, et al. Perspectives of Homo sapiens lifespan extension: focus on external or internal resources? *Ageing.* 2020;12:5566–84.

75. Somel M, Tang L, Khaitovich P. The role of neoteny in human evolution: from genes to the phenotype. In: Hirai H, Imai H, Go Y, editors. *Post-genome biology of primates*. Tokyo: Springer Tokyo; 2012. p. 23–41.
76. Somel M, Guo S, Fu N, et al. MicroRNA, mRNA, and protein expression link development and aging in human and macaque brain. *Genome Res*. 2010;20:1207–18.
77. Buffenstein R. The naked mole-rat: a new long-living model for human aging research. *J Gerontol A Biol Sci Med Sci*. 2005;60:1369–77.
78. Buffenstein R. Negligible senescence in the longest living rodent, the naked mole-rat: insights from a successfully aging species. *J Comp Physiol B*. 2008;178:439–45.
79. Buffenstein R, Amoroso VG. The untapped potential of comparative biology in aging research: insights from the extraordinary-long-lived naked mole-rat. Duque G (ed.). *J Gerontol A Biol Sci Med Sci*. 2024;79:glae110.
80. Ruby JG, Smith M, Buffenstein R. Five years later, with double the demographic data, naked mole-rat mortality rates continue to defy Gompertzian laws by not increasing with age. *GeroScience*. 2024. <https://doi.org/10.1007/s11357-024-01201-4>.
81. Holmes MM, Rosen GJ, Jordan CL, et al. Social control of brain morphology in a eusocial mammal. *Proc Natl Acad Sci*. 2007;104:10548–52.
82. Edrey YH, Park TJ, Kang H, et al. Endocrine function and neurobiology of the longest-living rodent, the naked mole-rat. *Exp Gerontol*. 2011;46:116–23.
83. Ruby JG, Smith M, Buffenstein R. Naked mole-rat mortality rates defy Gompertzian laws by not increasing with age. *eLife*. 2018;7:e31157.
84. Buffenstein R, Amoroso V, Andziak B, et al. The naked truth: a comprehensive clarification and classification of current ‘myths’ in naked mole-rat biology. *Biol Rev*. 2022;97:115–40.
85. Barker AJ, Vevurko G, Bennett NC, et al. Cultural transmission of vocal dialect in the naked mole-rat. *Science*. 2021;371:503–7.
86. Orr ME, Garbarino VR, Salinas A et al. Extended post-natal brain development in the longest-lived rodent: prolonged maintenance of neotenic traits in the naked mole-rat brain. *Front Neurosci*. 2016;10. <https://doi.org/10.3389/fnins.2016.00504>.
87. Dettmer AM, Chusyd DE. Early life adversities and life-long health outcomes: a review of the literature on large, social, long-lived nonhuman mammals. *Neurosci Biobehav Rev*. 2023;152:105297.
88. Wells RS. 2. Dolphin social complexity: lessons from long-term study and life history. In: De Waal FBM, Tyack PL, editors. *Animal social complexity*. Harvard University Press; 2003. pp. 32–56.
89. De Magalhães JP, Costa J. A database of vertebrate longevity records and their relation to other life-history traits. *J Evol Biol*. 2009;22:1770–4.
90. Gurven M, Kaplan H. Longevity among hunter-gatherers: a cross-cultural examination. *Popul Dev Rev*. 2007;33:321–65.
91. Lew-Levy S, Reckin R, Kissler SM, et al. Socioecology shapes child and adolescent time allocation in twelve hunter-gatherer and mixed-subsistence forager societies. *Sci Rep*. 2022;12:8054.
92. Davison R, Gurven M. The importance of elders: extending Hamilton’s force of selection to include intergenerational transfers. *Proc Natl Acad Sci*. 2022;119:e2200073119.
93. Pretelli I, Ringen E, Lew-Levy S. Foraging complexity and the evolution of childhood. *Sci Adv*. 2022;8:eabn9889.
94. Lawson DW, Uggla C. Family structure and health in the developing world: what can evolutionary anthropology contribute to population health science? In: Gibson MA, Lawson DW, editors. *Applied evolutionary anthropology*. Springer, New York: New York, NY; 2014. p. 85–118.
95. Brown SL, Brown RM. Connecting prosocial behavior to improved physical health: contributions from the neurobiology of parenting. *Neurosci Biobehav Rev*. 2015;55:1–17.
96. Kirkwood TBL. Why and how are we living longer?: Why and how are we living longer? *Exp Physiol*. 2017;102:1067–74.
97. Vila J. Social support and longevity: meta-analysis-based evidence and psychobiological mechanisms. *Front Psychol*. 2021;12:717164.
98. Cassel J. The contribution of the social environment to host resistance. *Am J Epidemiol*. 1976;104:107–23.
99. Cobb S. Social support as a moderator of life stress. *Psychosom Med*. 1976;38:300–14.
100. Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *Am J Epidemiol*. 1979;109:186–204.
101. Yang YC, Boen C, Gerken K, et al. Social relationships and physiological determinants of longevity across the human life span. *Proc Natl Acad Sci*. 2016;113:578–83.
102. Zhao M, Yang F, Zhang Y. The power of culture: the gendered impact of family structures and living arrangements on social networks of Chinese older adults. *Ageing Soc*. 2022;42:657–80.
103. Khan HTA. Factors associated with intergenerational social support among older adults across the world. *Ageing Int*. 2014;39:289–326.
104. Wong ELY, Liao JM, Etherton-Beer C, et al. Scoping review: intergenerational resource transfer and possible enabling factors. *Int J Environ Res Public Health*. 2020;17:7868.
105. Haberkern K, Szydlik M. State care provision, societal opinion and children’s care of older parents in 11 European countries. *Ageing Soc*. 2010;30:299–323.
106. Schenk N, Dykstra P, Maas I. The role of European welfare states in intergenerational money transfers: a micro-level perspective. *Ageing Soc*. 2010;30:1315–42.
107. Poulain M, Herm A, Errigo A, et al. Specific features of the oldest old from the Longevity Blue Zones in Ikaria and Sardinia. *Mech Ageing Dev*. 2021;198:111543.
108. Chrysohoou C, Pitsavos C, Lazaros G, et al. Determinants of all-cause mortality and incidence of cardiovascular disease (2009 to 2013) in older adults: the Ikaria study of the Blue Zones. *Angiology*. 2016;67:541–8.
109. Buettner D, Skemp S. Blue Zones: lessons from the world’s longest lived. *Am J Lifestyle Med*. 2016;10:318–21.

110. Engelbrecht H-R, Merrill SM, Gladish N, et al. Sex differences in epigenetic age in Mediterranean high longevity regions. *Front Aging*. 2022;3:1007098.
111. Panagiotakos DB, Chrysohoou C, Siasos G, et al. Sociodemographic and lifestyle statistics of oldest old people (>80 years) living in Ikaria Island: the Ikaria study. *Cardiol Res Pract*. 2011;2011:1–7.
112. Zamir A, Granek L, Carmel S. Factors affecting the will to live among elderly Jews living in Israel. *Aging Ment Health*. 2020;24:550–6.
113. Goto A, Yasumura S, Nishise Y, et al. Association of health behavior and social role with total mortality among Japanese elders in Okinawa. *Japan Aging Clin Exp Res*. 2003;15:443–50.
114. Vázquez-Palacios FR, Tovar-Cabañas R. Natural and cultural longevity zones from an anthropological and geographical viewpoint. *J Popul Ageing*. 2022;15:707–23.
115. Legrand R, Nuemi G, Poulain M, et al. Description of lifestyle, including social life, diet and physical activity, of people ≥90 years living in Ikaria, a longevity Blue Zone. *Int J Environ Res Public Health*. 2021;18:6602.
116. Fastame M, Hitchcott P, Mulas I, et al. Resilience in elders of the Sardinian Blue Zone: an explorative study. *Behav Sci*. 2018;8:30.
117. Buettner D. Blue Zones. *National Geographic*, 2009.
118. Poulain M, Pes GM, Grasland C, et al. Identification of a geographic area characterized by extreme longevity in the Sardinia island: the AKEA study. *Exp Gerontol*. 2004;39:1423–9.
119. Mori K, Kaiho Y, Tomata Y, et al. Sense of life worth living ( ikigai ) and incident functional disability in elderly Japanese: the Tsurugaya Project. *J Psychosom Res*. 2017;95:62–7.
120. Nakanishi N. “Ikigai” in older Japanese people. *Age Ageing*. 1999;28:323–4.
121. Zábó V, Csiszar A, Ungvari Z, et al. Psychological resilience and competence: key promoters of successful aging and flourishing in late life. *GeroScience*. 2023;45:3045–58.
122. Tanno K, Sakata K, Ohsawa M, et al. Associations of ikigai as a positive psychological factor with all-cause mortality and cause-specific mortality among middle-aged and elderly Japanese people: findings from the Japan Collaborative Cohort Study. *J Psychosom Res*. 2009;67:67–75.
123. Tomioka K, Kurumatani N, Hosoi H. Relationship of having hobbies and a purpose in life with mortality, activities of daily living, and instrumental activities of daily living among community-dwelling elderly adults. *J Epidemiol*. 2016;26:361–70.
124. Cohen S. Social relationships and health. *Am Psychol*. 2004;59:676–84.
125. MacLeod KJ, English S, Ruuskanen SK, et al. Stress in the social context: a behavioural and eco-evolutionary perspective. *J Exp Biol*. 2023;226:jeb245829.
126. Koenig JI, Walker C-D, Romeo RD, et al. Effects of stress across the lifespan. *Stress*. 2011;14:475–80.
127. Bangasser DA, Valentino RJ. Sex differences in stress-related psychiatric disorders: neurobiological perspectives. *Front Neuroendocrinol*. 2014;35:303–19.
128. Juster R-P, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev*. 2010;35:2–16.
129. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. *Psychol Bull*. 2011;137:959–97.
130. Myin-Germeys I, Krabbendam L, Delespaul PAEG, et al. Do life events have their effect on psychosis by influencing the emotional reactivity to daily life stress? *Psychol Med*. 2003;33:327–33.
131. Shields GS, Sazma MA, Yonelinas AP. The effects of acute stress on core executive functions: a meta-analysis and comparison with cortisol. *Neurosci Biobehav Rev*. 2016;68:651–68.
132. Shields GS, Trainor BC, Lam JCW, et al. Acute stress impairs cognitive flexibility in men, not women. *Stress*. 2016;19:542–6.
133. Silverman MN, Sternberg EM. Glucocorticoid regulation of inflammation and its functional correlates: from HPA axis to glucocorticoid receptor dysfunction. *Ann N Y Acad Sci*. 2012;1261:55–63.
134. Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. *Psychol Bull*. 2014;140:774–815.
135. Rosengren A, Orth-Gomer K, Wedel H, et al. Stressful life events, social support, and mortality in men born in 1933. *BMJ*. 1993;307:1102–5.
136. Gunnar MR, Hostinar CE. The social buffering of the hypothalamic–pituitary–adrenocortical axis in humans: developmental and experiential determinants. *Soc Neurosci*. 2015;10:479–88.
137. Brosschot J, Verkuil B, Thayer J. Generalized unsafety theory of stress: unsafe environments and conditions, and the default stress response. *Int J Environ Res Public Health*. 2018;15:464.
138. Thayer JF, Mather M, Koenig J. Stress and aging: a neurovisceral integration perspective. *Psychophysiology* 2021;58. <https://doi.org/10.1111/psyp.13804>.
139. Belyaev DK. Destabilizing selection as a factor in domestication. *J Hered*. 1979;70:301–8.
140. Darwin C. The variation in animals and plants under domestication. London: John Murray; 1868.
141. Hallowell AI, Boas F. The mind of primitive man. *Am Sociol Rev*. 1938;3:580.
142. Šimić G, Vukić V, Kopic J, et al. Molecules, mechanisms, and disorders of self-domestication: keys for understanding emotional and social communication from an evolutionary perspective. *Biomolecules*. 2020;11:2.
143. Wilkins AS, Wrangham RW, Fitch WT. The “domestication syndrome” in mammals: a unified explanation based on neural crest cell behavior and genetics. *Genetics*. 2014;197:795–808.
144. Hostinar CE, Sullivan RM, Gunnar MR. Psychobiological mechanisms underlying the social buffering of the hypothalamic–pituitary–adrenocortical axis: a review of animal models and human studies across development. *Psychol Bull*. 2014;140:256–82.
145. Lepore SJ. Problems and prospects for the social support-reactivity hypothesis. *Ann Behav Med*. 1998;20:257–69.
146. Uchino BN, Carlisle M, Birmingham W, et al. Social support and the reactivity hypothesis: conceptual issues in

- examining the efficacy of received support during acute psychological stress. *Biol Psychol.* 2011;86:137–42.
147. Dantzer B, Newman AEM, Boonstra R, et al. Density triggers maternal hormones that increase adaptive offspring growth in a wild mammal. *Science.* 2013;340:1215–7.
  148. Descamps S, Boutin S, Berteaux D, et al. Cohort effects in red squirrels: the influence of density, food abundance and temperature on future survival and reproductive success. *J Anim Ecol.* 2008;77:305–14.
  149. Thayer JF, Lane RD. Claude Bernard and the heart–brain connection: further elaboration of a model of neurovisceral integration. *Neurosci Biobehav Rev.* 2009;33:81–8.
  150. Wehrwein EA, Orer HS, Barman SM. Overview of the anatomy, physiology, and pharmacology of the autonomic nervous system. In: Terjung R, editor. *Comprehensive physiology.* 1st ed. Wiley; 2016. p. 1239–78.
  151. Porges SW. The polyvagal theory: new insights into adaptive reactions of the autonomic nervous system. *Cleve Clin J Med.* 2009;76:S86–90.
  152. Thayer JF, Lane RD. A model of neurovisceral integration in emotion regulation and dysregulation. *J Affect Disord.* 2000;61:201–16.
  153. Cené CW, Beckie TM, Sims M, et al. Effects of objective and perceived social isolation on cardiovascular and brain health: a scientific statement from the American Heart Association. *J Am Heart Assoc.* 2022;11:e026493.
  154. Valtorta NK, Kanaan M, Gilbody S, et al. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart.* 2016;102:1009–16.
  155. Minakata H. Oxytocin/vasopressin and gonadotropin-releasing hormone from cephalopods to vertebrates: Minakata. *Ann N Y Acad Sci.* 2010;1200:33–42.
  156. Gibbs DM. Vasopressin and oxytocin: hypothalamic modulators of the stress response: a review. *Psychoneuroendocrinology.* 1986;11:131–9.
  157. Purba JS. Increased number of vasopressin- and oxytocin-expressing neurons in the paraventricular nucleus of the hypothalamus in depression. *Arch Gen Psychiatry.* 1996;53:137.
  158. Meyerlindenberg A. Impact of prosocial neuropeptides on human brain function. *Progress in Brain Research.* Vol 170. Elsevier; 2008. pp. 463–70.
  159. Sue CC. Neuroendocrine perspectives on social attachment and love. *Psychoneuroendocrinology.* 1998;23:779–818.
  160. Crockford C, Deschner T, Wittig RM. The role of oxytocin in social buffering: what do primate studies add? In: Hurlemann R, Grinevich V, editors. *Behavioral pharmacology of neuropeptides: oxytocin*, vol. 35. Cham: Springer International Publishing; 2017. p. 155–73.
  161. Heinrichs M, Baumgartner T, Kirschbaum C, et al. Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol Psychiatry.* 2003;54:1389–98.
  162. Burtis CA, Ashwood ER, Bruns DE et al. *Tietz textbook of clinical chemistry and molecular diagnostics.* 5th ed. St. Louis, Mo.: Saunders; 2013.
  163. Donaldson ZR, Young LJ. The relative contribution of proximal 5' flanking sequence and microsatellite variation on brain vasopressin 1a receptor (Avpr1a) gene expression and behavior. *Nachman MW (ed.). PLoS Genet.* 2013;9:e1003729.
  164. Goodson JL, Bass AH. Social behavior functions and related anatomical characteristics of vasotocin/vasopressin systems in vertebrates. *Brain Res Rev.* 2001;35:246–65.
  165. Guastella AJ, Kenyon AR, Unkelbach C, et al. Arginine vasopressin selectively enhances recognition of sexual cues in male humans. *Psychoneuroendocrinology.* 2011;36:294–7.
  166. Insel TR. The challenge of translation in social neuroscience: a review of oxytocin, vasopressin, and affiliative behavior. *Neuron.* 2010;65:768–79.
  167. Kelly AM, Goodson JL. Functional significance of a phylogenetically widespread sexual dimorphism in vasotocin/vasopressin production. *Horm Behav.* 2013;64:840–6.
  168. Rigney N, de Vries GJ, Petrulis A, et al. Oxytocin, vasopressin, and social behavior: from neural circuits to clinical opportunities. *Endocrinology.* 2022;163:bqac111.
  169. De Vries GJ, Panzica GC. Sexual differentiation of central vasopressin and vasotocin systems in vertebrates: different mechanisms, similar endpoints. *Neuroscience.* 2006;138:947–55.
  170. Veenema AH, Bredewold R, De Vries GJ. Vasopressin regulates social recognition in juvenile and adult rats of both sexes, but in sex- and age-specific ways. *Horm Behav.* 2012;61:50–6.
  171. Albers HE. Species, sex and individual differences in the vasotocin/vasopressin system: relationship to neurochemical signaling in the social behavior neural network. *Front Neuroendocrinol.* 2015;36:49–71.
  172. Landgraf R, Neumann ID. Vasopressin and oxytocin release within the brain: a dynamic concept of multiple and variable modes of neuropeptide communication. *Front Neuroendocrinol.* 2004;25:150–76.
  173. Harper KM, Knapp DJ, Butler RK, et al. Amygdala arginine vasopressin modulates chronic ethanol withdrawal anxiety-like behavior in the social interaction task. *Alcohol Clin Exp Res.* 2019;43:2134–43.
  174. Rigney N, de Vries GJ, Petrulis A. Modulation of social behavior by distinct vasopressin sources. *Front Endocrinol.* 2023;14:1127792.
  175. Gabor CS, Phan A, Clipperton-Allen AE, et al. Interplay of oxytocin, vasopressin, and sex hormones in the regulation of social recognition. *Behav Neurosci.* 2012;126:97–109.
  176. Kany S, Vollrath JT, Relja B. Cytokines in inflammatory disease. *Int J Mol Sci.* 2019;20:6008.
  177. Booth A, Magnuson A, Fouts J, et al. Adipose tissue, obesity and adipokines: role in cancer promotion. *Horm Mol Biol Clin Investig.* 2015;21:57–74.
  178. Bunnell BA, Martin EC, Matossian MD, et al. The effect of obesity on adipose-derived stromal cells and adipose tissue and their impact on cancer. *Cancer Metastasis Rev.* 2022;41:549–73.
  179. Ghosh AK, O'Brien M, Mau T et al. Adipose tissue senescence and inflammation in aging is reversed by the young milieu. *Le Couteur D (ed.). J Gerontol Ser A.* 2019;74:1709–15.
  180. Police SB, Thatcher SE, Charnigo R, et al. Obesity promotes inflammation in periaortic adipose

- tissue and angiotensin II-induced abdominal aortic aneurysm formation. *Arterioscler Thromb Vasc Biol.* 2009;29:1458–64.
181. Stranahan AM. Visceral adiposity, inflammation, and hippocampal function in obesity. *Neuropharmacology.* 2022;205:108920.
  182. Csiszar A, Ungvari Z, Koller A, et al. Aging-induced proinflammatory shift in cytokine expression profile in rat coronary arteries. *FASEB J.* 2003;17:1183–5.
  183. Ungvari Z, Tarantini S, Sorond F, et al. Mechanisms of vascular aging, a geroscience perspective. *J Am Coll Cardiol.* 2020;75:931–41.
  184. Ungvari Z, Tarantini S, Donato AJ, et al. Mechanisms of vascular aging. *Circ Res.* 2018;123:849–67.
  185. Moieni M, Eisenberger NI. Effects of inflammation on social processes and implications for health. *Ann N Y Acad Sci.* 2018;1428:5–13.
  186. Muscatell KA, Moieni M, Inagaki TK, et al. Exposure to an inflammatory challenge enhances neural sensitivity to negative and positive social feedback. *Brain Behav Immun.* 2016;57:21–9.
  187. Eisenberger NI, Moieni M, Inagaki TK, et al. In sickness and in health: the co-regulation of inflammation and social behavior. *Neuropsychopharmacology.* 2017;42:242–53.
  188. Uchino BN, Tretzevik R, Kent de Grey RG et al. Social support, social integration, and inflammatory cytokines: a meta-analysis. *Health Psychol.* 2018;37:462–71.
  189. Furman D, Campisi J, Verdin E, et al. Chronic inflammation in the etiology of disease across the life span. *Nat Med.* 2019;25:1822–32.
  190. Chaib S, Tchkonja T, Kirkland JL. Cellular senescence and senolytics: the path to the clinic. *Nat Med.* 2022;28:1556–68.
  191. Tchkonja T, Kirkland JL. Aging, cell senescence, and chronic disease: emerging therapeutic strategies. *JAMA.* 2018;320:1319.
  192. Franceschi C, Garagnani P, Parini P, et al. Inflammaging: a new immune–metabolic viewpoint for age-related diseases. *Nat Rev Endocrinol.* 2018;14:576–90.
  193. Walker E, Ploubidis G, Fancourt D. Social engagement and loneliness are differentially associated with neuro-immune markers in older age: time-varying associations from the English Longitudinal Study of Ageing. *Brain Behav Immun.* 2019;82:224–9.
  194. Avitsur R, Powell N, Padgett DA, et al. Social interactions, stress, and immunity. *Immunol Allergy Clin North Am.* 2009;29:285–93.
  195. Segerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychol Bull.* 2004;130:601–30.
  196. Slavich GM, Way BM, Eisenberger NI, et al. Neural sensitivity to social rejection is associated with inflammatory responses to social stress. *Proc Natl Acad Sci.* 2010;107:14817–22.
  197. Cotter SC, Kilner RM. Personal immunity versus social immunity. *Behav Ecol.* 2010;21:663–8.
  198. Shattuck EC. Networks, cultures, and institutions: toward a social immunology. *Brain Behav Immun - Health.* 2021;18:100367.
  199. de Lombares C, Heude E, Alfama G, et al. Dlx5 and Dlx6 expression in GABAergic neurons controls behavior, metabolism, healthy aging and lifespan. *Aging.* 2019;11:6638–56.
  200. Levi G, de Lombares C, Giuliani C et al. DLX5/6 GABAergic expression affects social vocalization: implications for human evolution. Heyer E (ed.). *Mol Biol Evol.* 2021;38:4748–64.
  201. Schwarz F, Springer SA, Altheide TK, et al. Human-specific derived alleles of *CD33* and other genes protect against postreproductive cognitive decline. *Proc Natl Acad Sci.* 2016;113:74–9.
  202. López-Otín C, Blasco MA, Partridge L, et al. The hallmarks of aging. *Cell.* 2013;153:1194–217.
  203. Pal S, Tyler JK. Epigenetics and aging. *Sci Adv.* 2016;2:e1600584.
  204. Anier K, Malinovskaja K, Pruus K, et al. Maternal separation is associated with DNA methylation and behavioural changes in adult rats. *Eur Neuropsychopharmacol.* 2014;24:459–68.
  205. Provençal N, Suderman MJ, Guillemin C, et al. The signature of maternal rearing in the methylome in rhesus macaque prefrontal cortex and T cells. *J Neurosci.* 2012;32:15626–42.
  206. Weaver ICG, Cervoni N, Champagne FA, et al. Epigenetic programming by maternal behavior. *Nat Neurosci.* 2004;7:847–54.
  207. Laubach ZM, Greenberg JR, Turner JW, et al. Early-life social experience affects offspring DNA methylation and later life stress phenotype. *Nat Commun.* 2021;12:4398.
  208. McDade TW, Ryan C, Jones MJ, et al. Social and physical environments early in development predict DNA methylation of inflammatory genes in young adulthood. *Proc Natl Acad Sci.* 2017;114:7611–6.
  209. McDade TW, Ryan CP, Jones MJ, et al. Genome-wide analysis of DNA methylation in relation to socioeconomic status during development and early adulthood. *Am J Phys Anthropol.* 2019;169:3–11.
  210. Baker GT, Sprott RL. Biomarkers of aging. *Exp Gerontol.* 1988;23:223–39.
  211. Horvath S, Raj K. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. *Nat Rev Genet.* 2018;19:371–84.
  212. Horvath S. DNA methylation age of human tissues and cell types. *Genome Biol.* 2013;14:R115.
  213. Hannum G, Guinney J, Zhao L, et al. Genome-wide methylation profiles reveal quantitative views of human aging rates. *Mol Cell.* 2013;49:359–67.
  214. Levine ME, Lu AT, Quach A, et al. An epigenetic biomarker of aging for lifespan and healthspan. *Aging.* 2018;10:573–91.
  215. Lu AT, Quach A, Wilson JG, et al. DNA methylation GrimAge strongly predicts lifespan and healthspan. *Aging.* 2019;11:303–27.
  216. Belsky DW, Caspi A, Corcoran DL, et al. DunedinPACE, a DNA methylation biomarker of the pace of aging. *eLife.* 2022;11:e73420.
  217. Hamlat EJ, Prather AA, Horvath S, et al. Early life adversity, pubertal timing, and epigenetic age acceleration in adulthood. *Dev Psychobiol.* 2021;63:890–902.



218. McCrory C, Fiorito G, O'Halloran AM, et al. Early life adversity and age acceleration at mid-life and older ages indexed using the next-generation GrimAge and Pace of Aging epigenetic clocks. *Psychoneuroendocrinology*. 2022;137:105643.
219. Rampersaud R, Protsenko E, Yang R, et al. Dimensions of childhood adversity differentially affect biological aging in major depression. *Transl Psychiatry*. 2022;12:431.
220. Hillmann AR, Dhingra R, Reed RG. Positive social factors prospectively predict younger epigenetic age: findings from the Health and Retirement Study. *Psychoneuroendocrinology*. 2023;148:105988.
221. Simons RL, Lei MK, Beach SRH, et al. Economic hardship and biological weathering: the epigenetics of aging in a U.S. sample of black women. *Soc Sci Med*. 2016;150:192–200.
222. Hughes A, Smart M, Gorrie-Stone T, et al. Socio-economic position and DNA methylation age acceleration across the life course. *Am J Epidemiol*. 2018;187:2346–54.
223. Kiecolt-Glaser JK, Preacher KJ, MacCallum RC, et al. Chronic stress and age-related increases in the proinflammatory cytokine IL-6. *Proc Natl Acad Sci*. 2003;100:9090–5.
224. Niraula A, Witcher KG, Sheridan JF, et al. Interleukin-6 induced by social stress promotes a unique transcriptional signature in the monocytes that facilitate anxiety. *Biol Psychiatry*. 2019;85:679–89.
225. Needham BL, Adler N, Gregorich S, et al. Socio-economic status, health behavior, and leukocyte telomere length in the National Health and Nutrition Examination Survey, 1999–2002. *Soc Sci Med*. 2013;85:1–8.
226. Sherman GD, Mehta PH. Stress, cortisol, and social hierarchy. *Curr Opin Psychol*. 2020;33:227–32.
227. Bunea IM, Szentágotai-Táatar A, Miu AC. Early-life adversity and cortisol response to social stress: a meta-analysis. *Transl Psychiatry*. 2017;7:1274.
228. Ebner NC, Horta M, El-Shafie D. New directions for studying the aging social-cognitive brain. *Curr Opin Psychol*. 2024;56:101768.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.