Table 2
Comparison between the depressive (GDS ≥6) and non-depressive groups in each region.

	H in Korea (n=170)			D in Taiwan (n=164)			T in Japan (n=261)		
	GDS ≥6	GDS <6	P-value	GDS ≥6	GDS <6	P-value	GDS ≥ 6	GDS <6	P-value
Basic demography									
Age, mean (SD)	73.0 (5.2)	72.7 (5.4)	n.s.	75.3 (4.9)	73.3 (5.6)	.05	77.4 (5.9)	76.6 (6.4)	n.s.
Male, %	40.0	63.3	.003	50.0	59.1	n.s.	35.1	38.9	n.s.
Education, mean (SD)	4.5 (4.3)	6.0 (3.5)	n.s.	2.4 (2.6)	3.4 (3.2)	n.s.	6.3 (3.3)	6.6 (3.4)	n.s.
Activities of daily living, %									
Dependence on others for BADL	58.8	24.4	<.001	50.0	19.7	.001	29.8	13.8	.003
Socio-economic factors, %									
Living alone	26.2	7.8	.002	15.6	6.8	n.s.	22.2	18.4	n.s.
Loss of partner	41.2	17	.001	31.2	30.5	n.s.	34.9	34.0	n.s.
Sense of low economic status	35.0	15.7	.004	32.2	8.5	.002	57.0	20.2	<.001
Past medical history, %									
Stroke	7.6	7.9	n.s.	12.5	6.1	n.s.	14.9	6.4	.04
Cardiac disease	17.5	7.9	n.s.	28.1	20.5	n.s.	26.9	21.0	n.s.
Orthopedic disease	67.9	67.0	n.s.	25	43.5	n.s.	51.1	40.1	n.s.
Cancer	1.2	6.7	n.s.	0	0	NA	1.2	8.3	.04
Current medical condition, %									
Hypertension	43.8	34.4	n.s.	59.4	67.4	n.s.	61.7	60.2	n.s.
Diabetes mellitus	18.8	25.6	n.s.	34.4	28.8	n.s.	24.5	15.0	n.s.
Use of anti-hyperlipidemia medicine	7.5	1.1	n.s.	21.9	13.6	n.s.	24.1	14.8	n.s.
Use of anti-depressive medicine	5.0	1.1	n.s.	0	0	NA	8.4	0.6	.002
Use of hypnotic medicine	10.0	7.9	n.s.	25	3.0	<.001	33.7	24.4	n.s.
QOL subscales (0–100), mean (SD)									
Subjective health	51.4 (26.1)	65.5 ± 22.1	<.001	48.4 (17.3)	61.6 ± 21.5	.001	47.9 (18.4)	62.9 (16.9)	<.001
Family relationship	75.6 (23.6)	82.5 ± 19.4	.04	69.9 (19.3)	79.8 ± 17.9	.01	70.7 (22.7)	83.1 (14.2)	<.001
Friend relationship	71.0 (22.6)	72.8 ± 18.9	.02	72.3 (21.9)	73.9 ± 19.8	n.s.	70.7 (20.7)	80.9 (15.5)	<.001
Financial satisfaction	45.3 (24.3)	62.4 ± 25.3	<.001	42.8 (16.7)	57.0 ± 20.9	<.001	42.3 (23.0)	57.0 (19.9)	<.001
Subjective happiness	56.4 (25.8)	74.0 ± 22.9	<.001	50.2 (22.7)	72.1 ± 20.7	<.001	50.7 (20.2)	69.8 (15.5)	<.001

Student's t-test was used for continuous variables, the chi-squared test was used for categorical variables, and the Mann–Whitney U test was used for ordinal variables.

Table 3
Comparison of the odds ratios of confounding variables for GDS scores 6 or greater in logistic regression analysis among the three regions.

Variables	H in Korea (n=170)	P	D in Taiwan (n=164)	P	T in Japan (n=261)	P
Basic demography						
Education, years	0.93 (0.83–1.04)	n.s.	0.85 (0.71–1.01)	n.s.	0.98 (0.90–1.06)	n.s.
Activities of daily living						
Dependence on others for BADL	4.16 (2.05–8.45)	<.001	5.02 (1.96–12.85)	.001	2.73 (1.38–5.43)	.004
Socioeconomic risk factors						
Living alone	3.43 (1.33–8.86)	.01	2.05 (0.60–6.99)	n.s.	1.13 (0.58–2.21)	n.s.
Loss of partner	2.67 (1.20–5.95)	.02	0.92 (0.38–2.23)	n.s.	0.87 (0.45–1.70)	n.s.
Sense of low economic status	2.81 (1.33–5.96)	.007	4.67 (1.71–12.77)	.003	5.27 (2.96–9.37)	<.001
Past medical history						
Stroke	1.08 (0.33–3.50)	n.s.	2.00 (0.54–7.42)	n.s.	2.46 (1.02–5.94)	n.s.
Cardiac disease	2.47 (0.92–6.65)	n.s.	1.51 (0.62–3.71)	n.s.	1.40 (0.77–2.56)	n.s.
Orthopedic disease	0.84 (0.42–1.66)	n.s.	0.47 (0.19–1.15)	n.s.	1.51 (0.89–2.57)	n.s.
Cancer	0.23 (0.03–2.01)	n.s.	NA		0.15 (0.19–1.16)	n.s.
Current medical condition						
Hypertension	1.38 (0.73–2.63)	n.s.	0.65 (0.29–1.47)	n.s.	1.02 (0.60–1.73)	n.s.
Use of anti-hyperlipidemia medicine	8.39 (0.96–73.48)	n.s.	1.57 (0.58–4.26)	n.s.	1.74 (0.89–3.39)	n.s.
Diabetes mellitus	0.72 (0.34–1.54)	n.s.	1.29 (0.56–2.99)	n.s.	1.94 (1.02–3.68)	.04
QOL subscales						
Poor subjective health	2.65 (1.40–5.01)	.003	2.36 (1.02–5.48)	.045	4.34 (2.42–7.78)	<.001
Poor family relationship	1.60 (0.85–3.01)	n.s.	3.31 (1.40–7.81)	.006	2.47 (1.43–4.29)	.001
Poor friend relationship	2.29 (1.18–4.42)	.01	1.42 (0.64–3.15)	n.s.	2.32 (1.34–4.00)	.002
Low financial satisfaction	3.05 (1.59–5.87)	.001	4.48 (1.77–11.35)	.002	3.04 (1.76–5.25)	<.001
Low subjective happiness	4.00 (2.04–7.84)	<.001	5.78 (2.20–15.21)	<.001	5.16 (2.88–9.25)	<.001

All variables were adjusted for the effects of age and sex.

4. Discussion

In this study, we found that depressive state in the elderly was commonly associated with sense of low economic status as well as low scores for various QOL components and dependence in BADL in communities in three different Asian countries. Of particular note is that sense of low economic status and subjectively low QOL components were associated with depressive state in each community, even after adjusting for BADL dependence.

The highest percentage of individuals with a sense of low economic status was found in T town in Japan. Although the nominal gross domestic product of Japan is greater than those of the other two countries, people in Japan may feel that they have a lower economic status than do people in the other two countries, especially in depressive groups. Although poor economic situation is one of the risk factors for depression (Lorant et al., 2007), economic disparity may also influence the subjective sense of low economic status and the prevalence of depression (Kawachi & Kennedy, 1999). In fact, Japan has the highest Gini coefficient

Table 4
Comparison of the odds ratios of confounding variables for GDS scores 6 or greater in logistic regression analysis among the three regions.

Variables	H in Korea (n=170)	P	D in Taiwan (n=164)	P	T in Japan (n=261)	P
Socioeconomic factors						
Sense of low economic status	2.65 (1.21–5.82)	.02	4.53 (1.59–12.95)	.005	5.00 (2.79–8.94)	<.001
Loss of partner	2.96 (1.25–6.99)	.01	1.08 (0.42–2.74)	n.s.	0.82 (0.42–1.62)	n.s.
Living alone	3.48 (1.29–9.39)	.01	2.23 (0.61–8.09)	n.s.	1.07 (0.54–2.13)	n.s.
QOL subscales						
Poor subjective health	2.14 (1.10–4.19)	.03	2.21 (0.91–5.33)	n.s.	4.20 (2.33–7.57)	<.001
Poor family relationship	1.45 (0.75–2.81)	n.s.	3.21 (1.31–7.86)	.01	2.55 (1.46–4.47)	.001
Poor friend relationship	2.12 (1.06–4.22)	.03	1.56 (0.68–3.61)	n.s.	2.37 (1.36–4.11)	.002
Low financial satisfaction	2.97 (1.50–5.89)	.002	4.50 (1.71–11.86)	.002	2.90 (1.67–5.04)	<.001
Low subjective happiness	4.63 (2.23–9.61)	<.001	5.45 (2.03–14.68)	.001	5.13 (2.85–9.25)	<.001

All variables were adjusted for the effects of age, sex, and dependence on others for BADL.

(which is a measure of the inequality of a distribution, a value of 0 expressing total equality and a value of 1 maximal inequality) among the three countries studied (Japan 1993: 0.249; Japan 2008: 0.376; Korea 2000: 0.358; Korea 2010: 0.310; Taiwan 2000: 0.326) (International Monetary Fund, 2011). A study of country-level income inequality and depression among older Americans revealed that income inequality (evaluated by the Gini coefficient) was significantly associated with depression (Muramatsu, 2003); a similar phenomenon could occur in Asian countries (Chen et al., 2012). The factors affecting subjective sense of low economy should be investigated, and more attention should be paid to subjective sense of economy, as it is associated with depression and may lead to deterioration of physical and mental health in community-living elderly.

A previous Asian study, which included elderly people who were dependent in BADL, showed that depressive state was associated with all five QOL components (i.e., subjective health, family relationship, friend relationship, financial satisfaction, and subjective happiness) (Wada et al., 2005). Our study verified this result even after adjusting for the effects of BADL dependence. However, relationship with friends in D town in Taiwan and relationship with family in H town in Korea were not significantly associated with depressive state. This may indicate that financial satisfaction and subjective happiness were the common factors associated with depressive state or that the association between depressive state and human relationships, such as those between family and friends, differs between communities with different cultural backgrounds. Our results suggest that family relationships may be significant in Taiwan, whereas relationships outside the family may be appreciated more by Koreans. The sense of value of human relationship might differ between cultures; however, subjective sense of economic satisfaction might be commonly related with depressive mood in community-dwelling elderly across cultural differences. In fact, a comprehensive study on the QOL scale including 87 data sets incorporating data for 21,743 individuals clarified cultural differences in the relationship between total QOL score and each sub-score, including social functioning score (Scott et al., 2008). The study reported that social functioning score was a relatively less important predictor of overall QOL in Islamic countries, whereas in Latin America, it was the second-largest contributing predictor of overall QOL (Scott et al., 2008). As for Asia, in East Asia, social functioning score was reported to be slightly less predictive of overall QOL, but in South Asia, it tended to be predictive of overall QOL; however, this tendency was not significant (Scott et al., 2008). In any case, our study revealed that some components of QOL related to human relationships were preserved even in the depressive state, such as family relationship in Korea and friendship in Taiwan. This knowledge can be utilized in the provision of community-based healthcare or intervention against depressive states in the elderly.

Loss of partner and living alone were associated with depressive state only in H town in Korea; this seems to contradict the finding of no association between low family relationship QOL score and depressive state in H town.

A limitation of this study is the small sample size. The study's participants comprised 15.1% of the elderly population of T town in Japan, 29.9% of that of D town in Taiwan, and 10.5% of that of H town in Korea. The representativeness of the sample for D town in Taiwan and H town in Korea was relatively weak compared with that of T town in Japan. Although our results might underestimate the effects of the variables, common relationships between subjective economical satisfaction and depressive mood in the elderly may be true across different cultures.

5. Conclusions

Depressive state was associated with socioeconomic status, subjective QOL, and dependence in BADL in three Asian communities. The associations between depressive state and subjective sense of low economic status and subjective QOL were significant even after adjusting for the effect of BADL dependence. Although absolute and objective economic status are important contributing factors to depressive state or psychosocial deterioration, we should pay more attention to the role of "subjective sense" of low economic status in determining depressive state in community-dwelling elderly people in Asia.

Conflict of interest

The authors declare that they have no conflicts of interest.

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EDITORIAL

Geriatric issues from the standpoint of human evolution

Introduction

Mankind is thought to have separated from a common ancestor shared with chimpanzees approximately 7 million years ago.[1] At the time, among our ancestors was a group that decided to come down from the trees to live in the savanna as desertification of Africa's forests progressed. Although the term "ape-man" was used for early mankind who walked on two feet, improvements in the precision of dating methods and excavations from the latter half of the 20th century made it clear that many types of human species coexisted. Thus, the term "ape-man" is now only rarely used. Bipedalism was likely something attempted by many groups, and although many theories exist, the underlying reason for this transition is unclear.[2] However, the advantages are clear – it enabled viewing vast distances and the use of hands to carry food, and ultimately led to the expansion of brain size. Interestingly, it took our ancestors an additional 4 million years to expand their brain size. This evolutionary delay might have been caused by climate changes in Africa. The progressively drying climate led to reductions in forestland, and our ancestors who lived on the plains were subjected to a new type of natural selection pressure, causing changes in their physique and behavior. One possible reason that orangutans remained in the trees when transported to Asia by continental drift was that although Africa and the Northern hemisphere began to dry and cool from approximately 30 million to 2.5 million years ago, Asia's forests in the tropical regions remained intact.

Evidence of brain size expansion and the use of tools can be found from approximately 2.5 million years ago. Mankind at this stage is referred to as *Homo habilis* or *Homo rudolfensis*. The concept of pre-adaptation refers to gradually altering physique in advance so that it works to one's advantage once subjected to a particular environment. For instance, the advantages of walking erect are thought to have played an important role in the evolution of mankind much later; that is, approximately 2.5 million years later. The expansion of brain size also brought about a revolution in food energy, which accompanied the use of stone tools – the ability to ingest high caloric and nutritious meat products. Although they were "meat-eating" and hunted herbivorous animals on occasion, their meat supply likely came from food left over by carnivorous animals. In addition to increasing meat-eating efficiency, the expansion of brain size was accompanied by acquisition of modern man's physique, an expanded range of activity and loss of body hair.

Although many human species remained in Africa, one group, the Peking man or Java man (also known as *Homo erectus*) moved to Eurasia approximately 1.8 million years ago in an event referred to as the first African exodus. At least one group of *Homo erectus* began using fire, a monumental event in mankind's history. *Homo erectus* existed until 250 000 years ago.

We enter the age of modern man from approximately 200 000 years ago. The Neanderthals were another species of man that coexisted with modern humans during this period. This period saw the use of symbols, language and original art-forms. One group of modern humans left Africa approximately 100 000 years ago, and eventually adapted to all global environments in an event famously known as the second African exodus. Many terrains were conquered, including grasslands, deserts and mountains, and humans began living under various climates (tropical, temperate and polar). The conquering of various terrains is evidenced by the existence of Eskimos in polar regions, Bushmen in the deserts, Pygmies in the tropical rain forests, and Tibetan highlanders. The spreading of humans was particularly fast, with humans reaching Europe, Asia, North and South America, and Australia within the span of tens of thousands of years.

Mankind at the time formed small nomadic groups and lived as hunter-gatherers. From a modest population of approximately 100 000 about 1 million years ago, the global population dramatically increased to 500 000 about 200 000 years ago, and further to approximately 10 million with the advent of agriculture about 10 000 years ago.[3]

Dawning of the agricultural revolution

Domestication of wild plants and animals approximately 10 000 years ago was a groundbreaking event in mankind's history. With the introduction of agriculture, increased food production and storage became possible, and those not involved in food production became soldiers, bureaucrats, and technicians, evolving society and bringing about social and gender inequalities. As

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human cultures diversified further in the past 10 000 years or so, the divide between them also increased.

Lifestyle became settled with the advent of agriculture, naturally leading to explosive population growth. Indeed, this translated to a more than 10-fold increase in global population in the past 5000 years.

Agriculture also brought about new threats to mankind's existence. Although hunter-gatherers had difficulty securing an adequate food supply, they were able to maintain diversity in their diet with an appropriate variety of foods with respect to protein, mineral and vitamin intake. Agriculture, however, prompted the transition to carbohydrates as the main source of energy, leading to nutritional bias and malnutrition. Paleopathological studies comparing nutrition between hunter-gatherers and farmers suggest that hunter-gatherers likely led healthier lives.[4,5]

The reliance on a small amount of crops also made difficult the securing of adequate food supplies to support large populations, sometimes leading to famine. It is likely that the threats of malnutrition and famine were much more pronounced after the introduction of agriculture compared with when humans were hunter-gatherers.

In addition to the foregoing, diseases were also products of the agricultural revolution. Dense populations brought about epidemics. For instance, the concentration of people and livestock, and the introduction of irrigation provided mosquitoes ample hosts to spread infectious diseases. Infectious diseases were rampant among highly populated settled groups with poor nutritional status, transmitting from animal to human and from human to human. Epidemics were not an issue with hunter-gatherers, who remained in small groups and constantly travelled. Diseases that transmit between humans (e.g. tuberculosis, leprosy and cholera) became prominent with the introduction of agriculture. Smallpox, the bubonic plague and the measles came about in the past several thousands of years, as populations became concentrated with the building of cities. From the advent of agriculture to recent times, approximately one-fifth of the population is estimated to have died before the age of 5 years from malnutrition in infancy and infectious diseases. The history of epidemics since the agricultural revolution is discussed extensively in McNeill's *Plagues and People*.[3]

Since the times of Archimedes and Eratosthenes of Greece, scientists such as Copernicus, Newton, Galileo, Descartes and Leibniz have made revolutionary discoveries, but before the 18th century, there were no discoveries relating to evolution or findings that would form the basis for modern medicine. It was Jenner, at the end of the 18th century, who developed the smallpox vaccine and greatly influenced society through his keen, experienced intuition.

Although the human population grew explosively with the advent of agriculture, it is estimated that the total population from Ancient Greece to the Roman period, and further through the period of explosive population growth that accompanied the period when agriculture became firmly rooted in society, was approximately 100 million or so.

Since the agricultural life became fixed a few thousand years ago until about 1700, there was no dramatic increase in population.

Evolutionary significance of lifestyle-related diseases

For at least the 6.99 million years since humans diverged from their chimpanzee ancestors 7 million years ago, our bodies were designed to live in small groups as hunter-gatherers. Genes maximally adapted the human body to the environment and lifestyle of the Stone Age by establishing an immune system to fight infectious diseases, hemostasis mechanisms to minimize bleeding from wounds, an energy-saving mechanism to overcome starvation, and neuro- and muscular-response systems to allow for strenuous movements. At most, the lifespan of an adult in the Stone Age was 30–40 years, and the body was designed to adapt to this lifespan. With agriculture and the transition to a settled lifestyle came the densification of populations; however, this transition was not accompanied by a substantial increase in lifespan.

However, substantial changes in mankind's history were brought about in the latter 50 years of the 20th century. Stabilization of the food supply curbed starvation, and brought about satiation. Food composition transitioned from a carbohydrate-based diet to being protein- and fat-based. Changes in industrial structure brought about transition to a sedentary lifestyle, accompanied by lack of exercise, from a physical labor-based agricultural lifestyle. Yet, the greatest change was the marked increase in human lifespan. Indeed, the human body, which was maximally adapted to the Stone Age, would experience a lifespan of 80–90 years for the first time.

Fats, sugars and salt were constantly lacking in mankind's history. Humans had a lifespan of 30–40 years, and taking in as much of these substances as possible was considered healthy. However, as these substances became plentiful, the incidence of high blood pressure, and subsequent stroke, increased after the age of 40 years. Similarly, with satiation, the energy-saving mechanism designed to withstand starvation led to diabetes. The cholesterol system, which stores and effectively uses fat when the food supply is low, led to deposition of cholesterol in blood vessels after the age of 40 years, causing atherosclerosis and myocardial infarction. Colon cancer is also increasing at an alarming pace as a result of high fat diets and prolonged lifespan. The mechanism of calcium intake into bones during growth led to calcium deposition in blood vessels after middle age, promoting atherosclerosis.

Recently, gene polymorphisms that influence the development of chronic diseases, myocardial infarction and osteoporosis in the elderly are being identified one after another. Yet, these polymorphisms might be performing useful functions in younger years. The age-related "biological trade-off", wherein the effects are favorable when young, but become detrimental with aging, is easy to understand when considered from the evolutionary context.

The various lifestyle-related diseases faced by developed countries likely reflect the surpassing of the capacity of the human body, which was adapted to the 30 to 40-year lifespan of the Stone Age, due to rapid environmental changes and the extension of lifespan. Fifty years is obviously much too short a period for genes to evolutionarily adapt and promote changes to the human body.

Trade-offs from bipedalism and brain size expansion: Fractures, falls and cognitive disorders

The genetic design acquired by mankind over its 7 million-year evolutionary history was designed to adapt to Africa's ecosystem and environment. Acquiring the ability to walk on two feet was a paradigm-changing event. To achieve this feat, humans needed to morphologically alter the pelvis and acquire the complex ability of balancing. From the standpoint of human developmental ontogeny, the ability to achieve stable body balance requires many years of growth from infancy. Yet, this ability declines with the progression of age in the older years. It is unlikely that genes could have foreseen that 7 million years later, bipedalism would lead to falls and fractures in the elderly, which rank third among reasons that elderly people become bedridden.

Approximately 4 million years after beginning to walk on two feet, the brain size expanded, which led to the invention of stone tools, the first African exodus, the use of fire, the second African exodus, the invention of language, development of art-forms and the invention of agriculture. Since the agricultural revolution, humans have continuously altered the global environment. While increasing population density by adopting a settled lifestyle, some also sought farmlands and pasturelands, moving to and seeking livelihoods in various environments. By taking advantage of the natural ecosystem of a particular terrain, they established cities and inter-regional trade networks, creating a human-specific social structure called "civilization", and contemplating even the well-being of the spiritual world. All of these were brought about by the developed brain, which finds no equal in other animals. One can go as far as saying that modern political/economical systems, environmental health systems and the development of modern medicine were not products of genetic design, but rather brought about by civilizations, using the human brain as a vehicle.

As aforementioned, the genetic design that presumed a lifespan of 30–40 years likely did not expect the modern lifespan of 90 years. The evolution of intellectual ability that accompanied brain expansion, and the resulting super-aged human societies, will come to experience Alzheimer's disease as a common disease. Bipedalism versus falls in the elderly years, and brain expansion versus cognitive disorders in the elderly are representative biological trade-offs; that is, abilities that were advantageous in younger years, but function detrimentally in the elderly.

Conclusion

The basic principle in the evolution of life was "to live long enough to reproduce." Yet, 21st century humans are faced with a problem that transcends this principle, namely, "living much longer after reproduction." When considering the basis of survival of the anthroposphere, in addition to issues related to energy and the global environment, one task moving forward will be how to construct the advancing elderly society. While we have experienced the greatest scale of population increase since the agricultural revolution and the first major extension of lifespan in human history, the "cultural" genes of mankind will be faced with more problems related to survival than the many that have been experienced to date.

Elderly persons living a satisfying, purposeful life followed by a peaceful death is the ideal, but it poses a challenge as to whether we are able to create a society in which this can be achieved.[6,7]

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Kozo Matsubayashi
Center for Southeast Asian Studies, Kyoto University, Kyoto, Japan

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COMPREHENSIVE GERIATRIC ASSESSMENT REVEALS SLEEP DISTURBANCES IN COMMUNITY-DWELLING ELDERLY ADULTS ASSOCIATED WITH EVEN SLIGHT COGNITIVE DECLINE

To the Editor: Advancing age is commonly associated with greater likelihood of sleep disturbances and cognitive impairment. Many studies[1–4] show strong associations between sleep quality and cognition in older adults with dementia and with mild cognitive impairment. Few studies examined sleep quality in older community-dwelling people with only slightly impaired cognition (Mini-Mental State Examination (MMSE) score ≥25). Sleep disturbances in older adults may be less a function of age per se and more a function of other factors accompanying aging.[5] A community-based geriatric assessment of elderly adults[6] was performed to investigate whether there were significant associations between mild cognitive decline and poor sleep quality indicators in older citizens in a rural Japanese town.

The study population consisted of 691 individuals aged 75 to 102 (male:female 237:454, mean age 81.0 ± 4.6) living in a rural Japanese town (Tosa, Kochi prefecture). Participants had scores of 25 or above on the MMSE (range 0–30). They were classified into three classes according to MMSE score (29–30, n = 282, aged 80.5 ± 4.2; 27–28, n = 219, aged 81.5 ± 4.6; 25–26, n = 190, aged 81.0 ± 4.9; Table 1). Hasegawa Dementia Rating Scale-Revised (range 0–30) were 28.5 ± 2.0, 27.1 ± 2.2 and 26.2 ± 2.5, respectively, for each MMSE group, and Frontal Assessment Battery (range 0–18) scores were 13.5 ± 2.4, 12.5 ± 2.7 and 11.7 ± 2.4 for each MMSE group, respectively. Scores were lower with lower MMSE score.

A self-reported questionnaire assessed sleep characteristics. Average total sleep time was 7.99 ± 1.22 hours, time of getting-up was 5:59 ± 0:47, and time of going to bed was 21:58 ± 1:07. Feeling of poor-quality sleep (18.3%), use of sleep medication (28.7%), nocturnal waking for urination (79.4%; ≥2 times 16.3%), trouble falling asleep after nocturnal waking (36.3%), waking too early (29.2%), and waking not rested (44.6%) were reported.

Sleep complaints (feeling of poor-quality sleep, use of sleep medication, difficulty maintaining sleep, waking too early, waking not rested, daytime napping) were not statistically significantly associated with cognition. Elderly adults with lower MMSE scores slept longer (7.86, 7.97, and 8.22 hours, respectively; P = .008) and had more-frequent episodes of nocturia (1.65, 1.83, and 2.01 times, respectively; P = .006), in keeping with results from previous studies.[5,7]

The incidence of restless legs syndrome, sleep paralysis, sleep talking, and teeth-grinding were not statistically significantly different between the three MMSE groups, but fewer subjects with lower MMSE scores reported leg cramps (39.9%, 34.7%, and 30.4%, respectively; P = .03) and snoring (38.2%, 40.4%, and 29.6%, respectively; P = .06).

Several clinical signs were reported during sleep: waking from dry mouth (12.9%), nocturnal palpitation (2.2%), vague chest anginal discomfort (1.9%), and heartburn (5.1%). Only awakening from vague chest discomfort was less frequent in participants with higher MMSE scores (0.4%, 3.2%, and 2.7%, respectively; P = .04).

Previous studies showed an association between depressive mood and subjective quality of life (QOL),[6,8] but in this investigation, there were no differences in

Table 1. Associations Between Mini-Mental State Examination (MMSE) and Subjective Sleep Symptoms, Depression, Quality of Life (QOL), Physical Function, and Cardiovascular Function in Elderly Adults in a Rural Japanese Town

Characteristic	Total, N = 691	MMSE 29–30, n = 282	MMSE 27–28, n = 219	MMSE 25–26, n = 190	P-Value
Age, mean ± SD	81.0 ± 4.6	80.5 ± 4.2	81.5 ± 4.6	81.0 ± 4.9	.08
Female, %	65.7	68.4	65.3	62.1	.36
Body mass index, kg/m², mean ± SD	22.9 ± 3.5	23.1 ± 3.5	22.5 ± 3.4	23.0 ± 3.4	.36
MMSE score, mean ± SD	27.8 ± 1.7	29.5 ± 0.5	27.5 ± 0.5[a]	25.5 ± 0.5[b,c]	<.001
Hasegawa Dementia Rating Scale—Revised, mean ± SD	27.5 ± 2.4	28.5 ± 2.0	27.1 ± 2.2[a]	26.2 ± 2.5[b,c]	<.001
Frontal Assessment Battery, mean ± SD	12.7 ± 2.6	13.5 ± 2.4	12.5 ± 2.7[a]	11.7 ± 2.4[b,c]	<.001
Sleep duration, hours, mean ± SD	7.99 ± 1.22	7.86 ± 1.14	7.97 ± 1.28[a]	8.22 ± 1.24[b,c]	.008
Feeling of poor sleep quality, %	18.3	15.1	22.6	18.0	.11
Medicine for sleep, %	28.7	30.9	26.4	28.1	.54
Nocturnal waking, %	20.6	75.8	82.5	81.2	.15
Number of nocturia episodes per night, mean ± SD	1.81 ± 0.93	1.65 ± 0.83	1.83 ± 0.87[a]	2.00 ± 1.07[b]	.006
Trouble falling asleep after nocturnal waking, %	36.3	33.7	40.2	35.5	.33
Waking too early, %	29.2	29.6	30.5	27.0	.73
Waking not rested, %	44.6	43.4	42.6	48.3	.50
Restless legs, %	20.3	18.5	23.4	19.4	.38
Leg cramps, %	35.7	39.9	34.7	30.4[e]	.03
Increased dream, %	18.4	16.3	17.0	23.0	.15

(*Continued*)

Table 1 (Contd.)

Characteristic	Total, N = 691	MMSE 29–30, n = 282	MMSE 27–28, n = 219	MMSE 25–26, n = 190	P-Value
Sleep paralysis, %	5.9	4.7	5.5	8.2	.29
Sleep talking, %	14.3	13.5	14.4	15.7	.80
Teeth-grinding	4.3	4.0	6.0	2.7	.25
Snoring, %	36.5	38.2	40.4	29.6[f]	.06
Waking from dry mouth, %	12.9	10.9	16.5	11.8	.16
Waking from hunger, %	2.2	1.5	3.2	2.1	.42
Waking from shortness of breath, %	3.5	2.5	4.6	3.7	.45
Waking from asthma-like episode, %	2.6	2.5	2.8	2.7	.98
Waking from palpitation, %	2.2	2.5	1.4	2.7	.59
Waking from vague chest anginal discomfort, %	1.9	0.4	3.2[d]	2.7[e]	.04
Nocturnal heartburn, %	5.1	3.6	5.5	6.9	.28
Waking from abdominal pain, %	2.2	2.9	2.8	0.5	.18
Waking from back pain, %	6.2	4.7	6.9	7.5	.41
Daytime napping, %	48.7	52.0	48.4	44.1	.25
Duration of daytime napping, minutes, mean ± SD	30.2 ± 34.0	30.4 ± 33.2	28.2 ± 30.6	32.4 ± 38.9	.62
Habit of daytime exercise, %	51.5	54.6	48.8	50.0	.40
Duration of exercise, minutes, mean ± SD	90.5 ± 100.6	86.4 ± 81.6	96.1 ± 113.9	92.1 ± 117.1	.56
Depressive mood, %	47.8	33.9	37.0	37.4	.68
Frequency of depression, %	15.3	12.0	12.8	13.5	.91
Subjective quality of life, mean ± SD					
Health	57.7 ± 20.2	57.8 ± 21.4	56.4 ± 19.6	59.2 ± 19.0	.75
Family relationships	79.9 ± 20.0	81.3 ± 20.2	79.8 ± 18.4	77.5 ± 21.8	.55
Relationships with friends	77.0 ± 20.1	79.6 ± 18.4	74.8 ± 22.6	75.4 ± 19.4	.26
Financial satisfaction	57.8 ± 23.5	57.0 ± 24.7	58.4 ± 23.1	58.5 ± 22.0	.90
Happiness	65.2 ± 21.8	65.1 ± 23.2	66.7 ± 21.8	63.6 ± 19.3	.75
Systolic blood pressure, mmHg, mean ± SD	137.4 ± 19.3	137.8 ± 20.0	136.6 ± 19.8	137.8 ± 17.8	.74
Diastolic blood pressure, mmHg, mean ± SD	75.1 ± 11.0	74.7 ± 11.1	75.0 ± 10.7	75.7 ± 11.1	.64
Pulse, beats/min, mean ± SD	67.4 ± 11.2	67.1 ± 11.5	67.7 ± 10.5	67.6 ± 11.7	.83
Orthostatic hypotension, %	10.6	7.5	11.0	14.7[e]	.01
Orthostatic hypertension, %	9.7	7.1	10.1	13.2[e]	.03
Blood oxygen saturation, mean ± SD	96.2 ± 1.5	96.2 ± 1.5	96.1 ± 1.6	96.3 ± 1.5	.48
Respiration rate, number per min, mean ± SD	18.3 ± 3.9	18.2 ± 3.8	18.1 ± 3.9	18.6 ± 4.1	.50
Frequency of electrocardiographic ST-T changes, %	30.3	24.7	26.8	20.3	.40
Electrocardiographic QRS amplitude (SV1 + RV5), mm, mean ± SD	25.7 ± 8.7	25.8 ± 8.7	25.6 ± 8.7	25.7 ± 8.7	.97
Medicine for hypertension, %	64.9	70.4	64.1	56.4[e]	.01
Medicine for type 2 diabetes mellitus, %	5.8	6.6	4.3	6.4	.64
Timed Up & Go test, seconds, mean ± SD	12.6 ± 3.9	12.0 ± 4.0	13.0 ± 4.1[a]	12.9 ± 3.2[b]	.004
Handgrip power, kg, mean ± SD	22.3 ± 7.5	22.8 ± 7.1	21.7 ± 8.0	22.2 ± 7.6	.27
Time standing on single leg, seconds, mean ± SD	24.2 ± 20.6	27.9 ± 21.2	23.5 ± 21.3[a]	19.5 ± 17.4[b,c]	<.001
Functional reach, cm, mean ± SD	25.9 ± 7.4	26.8 ± 7.5	25.6 ± 7.3	24.9 ± 7.1[b]	.02
Button test, seconds, mean ± SD	13.9 ± 4.6	13.4 ± 4.9	14.0 ± 3.9	14.5 ± 4.9[b]	.003

$P < .05$ according to Student t-test between [a]MMSE 29–30 and 27–28; [b]MMSE 29–30 and 25–26; [c]MMSE 27–28 and 25–26.
$P < .05$ according to chi-square between [d]MMSE 29–30 and 27–28; [e]MMSE 29–30 and 25–26; [f]MMSE 27–28 and 25–26.
SD = standard deviation.

depressive mood and five QOL items (health, relations with family and friends, financial income, happiness) between the three MMSE groups.

Nor were differences between the three MMSE groups found in terms of blood pressure, pulse, respiration rate, blood oxygen saturation, QRS amplitude of electrocardiogram showing left ventricular mass volume, and ST-T changes suggesting myocardial ischemia. In keeping with a previous report,[9] blood pressure coordination (orthostatic hypotension or hypertension), along with indicators of standing behavior, deteriorated in subjects with lower MMSE scores (14.6%, 21.1%, and 27.9%, respectively; $P < .001$), who were less likely to be treated for hypertension.

Physical function was also assessed. Poorer function was associated with lower MMSE score, perhaps another reason for disordered sleep. Ability to perform such tests as the Timed Up & Go ($P = .004$), functional reach ($P = .02$), time standing on single leg ($P < .001$), and button score ($P = .003$) (but not handgrip power) declined with MMSE decreasing score (from 30 to 25).

Even though decline in cognitive function was minimal in the current study, the findings suggest that changes were already occurring in sleep characteristics. Total sleep time lengthened, and increases in nocturia caused sleep disturbances. Clinical symptoms started developing, such as chest pain, orthostatic hypotension, and orthostatic hypertension. A comprehensive geriatric assessment should be undertaken in older adults to determine any changes in cognitive function and prevent the development of insomnia-related diseases, if cognitive changes indeed precede rather than follow[10] decline in sleep quality.

Kuniaki Otsuka, MD
Chronomics and Gerontology, Tokyo Women's Medical University, Arakawa-ku, Tokyo, Japan

Germaine Cornelissen, PhD
Halberg Chronobiology Center, University of Minnesota, Minneapolis, Minnesota

Takashi Yamanaka, MD
Sachiko Oinuma, MD
Junko Sasaki, MA
Home Medical Care, Medical Center East, Tokyo Women's Medical University, Arakawa-ku, Tokyo, Japan

Gaku Yamanaka, MD
Department of Medicine, Medical Center East, Tokyo Women's Medical University, Arakawa-ku, Tokyo, Japan

Kiyohito Okumiya, MD
Department of Field Medicine, Research Institute for Humanity and Nature, Kamigyo-ku, Kyoto, Japan

Kozo Matsubayashi, MD
Department of Field Medicine, Center for Southeast Asian Studies, Kyoo University, Kyoto, Japan

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GERIATRIC INCLUSIVE ART AND RISK OF IN-HOSPITAL MORTALITY IN INPATIENTS WITH DEMENTIA: RESULTS FROM A QUASI-EXPERIMENTAL STUDY

To the Editor: The risk of in-hospital mortality is high in older inpatients with dementia because of multiorgan impairments due to comorbidities.[1] Emotional well-being may improve survival in older community-dwellers.[2,3] It has been reported that geriatric inclusive art (GIA), a new form of art therapy for older inpatients, reduces the length of hospital stay.[4] GIA uses painting to make inpatients aware of their abilities through improvement in emotional well-being. Because GIA may improve emotional well-being, and emotional well-being may reduce the risk of mortality among older community-dwellers, it was hypothesized that GIA could reduce in-hospital mortality in older inpatients with dementia. The objective of the study was to determine whether a GIA session performed in individuals with dementia hospitalized in a geriatric acute care unit could reduce in-hospital mortality.

Fifty-five individuals with dementia who participated in one GIA session and 73 paired controls with dementia, matched on age, sex, living situation (community vs nursing home), and reasons for hospitalization, hospitalized in the geriatric acute care unit of Angers University Hospital, France, were prospectively included in 2012 in this quasi-experimental study. Information was collected at admission on age, sex, body mass index (BMI, kg/m^2), regular physical activity (≥ 1 recreational physical activity for ≥ 1 hour per week for the past month or longer), comorbidity burden measured using the Cumulative Illness Rating Scale for Geriatrics (CIRS-G),[5] history of two or more recurrent falls during the past 6 months, dementia stage (Mini-Mental State of Examination (MMSE) score 20–25 = mild; MMSE score 10–19 = moderate; MMSE score <10 = severe),[6] presence of depressive symptoms defined as a 4-item Geriatric Depression Scale (GDS) score of 1 or greater,[7] feeling of physical or psychological weakness (being tired ≥ 3 days a week), and reasons for admission to a geriatric acute care unit (acute organ failures vs other). Information was obtained from the participant or from a close person living with the participant. In-hospital mortality and length of hospital stay were recorded in number of days from the administrative registry of Angers University Hospital. Participation in a GIA session was defined as painting a picture under the supervision of a moderator and a nurse. Each participant participated in one session during his or her hospital stay, with a maximum of four individuals attending a session at once. Sessions lasted 90 minutes. The Angers ethics committee approved the project. Individuals with dementia were

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Global Environmental Issues from the Viewpoints of Medical Surveys on Non-Caucasian Highlanders in the World

Kozo Matsubayashi[1)] and Kiyohito Okumiya[2)]

1) Center for Southeast Asian Studies, Kyoto University
2) Research Institute for Humanity and Nature

Introduction

A big project entitled " Human Life, Aging, and Diseases in High-Altitude Environments: Physio-Medical, Ecological and Cultural Adaptation in Highland Civilizations" lead by Kiyohito Okumiya in Research Institute for Humanity Nature in Kyoto, Japan has carried out during 8 years and finished in 2013. The achievements of this projects included 201 original articles and 3 books until now.

The contemporary brief summaries were reported in the Editorial of *Himalayan Study Monographs* volume *12, 13, 14,* respectively.[1,2,3)] And medical summary of the project will be published by the project leader Kiyohito Okimiya elsewhere.

At the end of the project, Editors try to view the points of the global environmental issues in the world from the standpoints of long-term evolutionary timespan based on the findings and discussions we obtained throughout the project.

Non-Caucasian Highlander's Lifestyle and Environments

As researchers who study highlanders living in hypoxic environments, we ourselves, of course, need to adapt to the highland environment. Most members of our team suffer from the symptoms of high altitude sickness when moving from sea level to the highlands, but gradually acclimate to the low oxygen. Even after adapting to the new environment, our breathing becomes labored when handling heavy loads. We cannot help but feel intrigued by the mystery of hypoxic adaptation achieved through evolution over a vast period, as well as the deep religious faith, of Tibetans who travel tens of kilometers, while repeatedly prostrating themselves, as they make pilgrimages to the holy mountains.

Compared to the fleeting human lifespan of less than a hundred years, the silver peaks of the Himalayas visible far away, which have surely been in existence for the past several million years, appear unchanging in their eternal form. Highlanders have continued to look to the Himalayan peaks for generations, revering and passing on to future generations their holy existence.

Migrating birds forming a full arc, leisurely flying above the Himalayas and taking a lengthy lakeside rest at an altitude of 4000 meters, prompt the following question: "How did they manage to adapt to this hypoxic environment?"

Highlanders who farm and herd morning to evening, sheep and yac herds that freely graze, Himalayan peaks that shine brightly in the blue sky and form the distant scenery of highland villages, gulls that dance in the firmament-these are all part of the typical highland scenery. Only here does it seem that time flows slowly. Life-of humans, animals, and plants-and the ecological and cultural environments that form the Earth come together, linked by the keyword "hypoxia," as a single archetype within the global frontier known as the highlands.

We have touched on the fact that a vast period of time was needed for highlanders to genetically adapt to the hypoxic highland environment and, at the same time, establish the sphere of daily living. They exercised ingenuity toward their livelihood and brought about cultural adaptations, such as the sharing of religion as a spiritual entity. Over the past several thousands of years, highlanders have led a stable existence in this harsh ecological environment. These highlanders are all non-Caucasian people. Yet, recent years have brought marked changes to their lives, changes that have been discussed primarily in terms of medical findings. Changes in nature-human interactions brought about by mutual influences between the global environment and human action, are thought to arise in most radical form at the Earth's ecological frontiers, which are characterized by unique natural ecosystems. It is now clear that the genetic adaptations that allowed highlanders to the adapt to the hypoxic environment throughout life (over the course of birth, development, and middle age) act to advance the pace of developing lifestyle-related diseases, such as diabetes, particularly in view of longer lifespans.

Biological trade-offs are phenomena in which genetic factors that worked to one's benefit in youth become detrimental at older ages. Relationships between hypoxic adaptation, older age, and lifestyle-related diseases become much clearer in the highlands. The most important issue, however, is that once discovered, lifestyle improvements allow for the management or prevention of lifestyle-related diseases attributed to genetic factors implicated in biological adaptation. It is never too late.

By construing genetic adaptation to the global environment and its result as "the global environment etched onto the human body," we have found alterations in the interplay between the global environment, the anthroposphere and animal/plant life, reflected in the aging of highlanders. If we assert that alterations in the interrelationship between the three spheres forming the global system (anthroposphere, biosphere, and geosphere) are reflected in human diseases and aging in the form of 'global environmental issues,' the study of highlanders has provided us with an important awareness of these issues.

While global environmental problems are important issues to be faced by mankind in the next 50 years or so, they must be considered on both spatial (from the microscopic gene level to the unit/group level) and temporal (the 4.6 billion years of Earth's history, 4 billion years of biological evolution, and mankind's 7 million year history) scales when contemplating their essence.

Construing "global environmental issues"

Although global environmental issues are regarded as problems of the compounded and complex sort that must be studied on multiple levels, the preface of the Encyclopedia of Global Environmental Studies simply lays them out as, "in the context of Earth-anthroposphere interactions, a group of 'problems' in which environmental changes that carry the risk of drastically stressing the environment to the extent of threatening the realm of life are seen as problematic, and for which an agreement to take preventative measures based on scientific prediction is in the process of being developed." Such an understanding places strong focus on the reality that global environmental changes brought about by humans alter the Earth's physical factors and ecosystems, and this change threatens the conditions for mankind's existence. These are urgent issues that have instilled fear in the human race over the past few decades.

For the time being, we classify global environmental issues based on the three spheres of geosphere, biosphere, and anthroposphere. When considering these issues in the context of adaptation, maladaptation, over-adaptation, and discord resulting from the interaction between these three spheres, various broader aspects of global environmental issues come to light.

Geosphere-anthroposphere interactions

Our awareness regarding global environmental issues begins, for the most part, from concerns about various problems arising from geosphere-anthroposphere interactions. The damage attributed to and influence of global environmental issues, first of all, are not limited to a single country of origin, but rather spread past national borders, expanding to the global scale. Addressing global environmental issues originating in developing countries requires concerted global efforts involving advanced countries as well. Recent noteworthy issues include destruction of the ozone layer, global warming, acid rain, transboundary movement of hazardous waste, water pollution, rain forest deforestation, desertification, exhaustion of fossil fuels, and pollution in developing countries. These issues have become more severe due to the social structure of mass production, mass consumption, and mass disposal in advanced countries, and population increases and the associated stress on environmental resource use in developing countries. Since these issues have the potential to greatly influence the survival and prosperity of mankind, they have been raised as issues of utmost importance in international politics. All of these factors are alterations to the global environment resulting from human production activities and consumption behavior, and their impact is beginning to be felt around the world.

In order to consider global environmental issues at the most fundamental level, as symbolized by biodiversity, a discussion of the 4 billion year history of the biosphere from a multilayered and wide angled perspective is warranted.

Geosphere-biosphere interactions

The signs of primitive life can be seen from about 4 billion years ago, and the biosphere existed throughout this period as a presence that tirelessly altered cells and genes to facilitate the adaptation to physical and chemical changes in the global environment. This process is called evolution. Only those species that adapted to the global environment were allowed to survive and propagate, and those that failed to adapt or overadapted went extinct.

We are inclined to think that this world was always as we see it now. When considering global environmental issues, we are prone to the mistaken impression that the global environment is invariable. While it is common knowledge that the Earth was covered in magma 4.6 billion years ago, it is difficult for us to grasp the subsequent environmental changes that occurred.

For example, it was thought until the 19th century that the positioning of Earth's landmasses was unchanged since the beginning of life history. The German geophysicist Alfred Wegener realized that continents far apart, such as South America and Africa, had land shapes that could be fit together like jigsaw puzzle pieces. When he proposed the continental drift theory in 1912, many scholars dismissed his views. We now know that when dinosaurs came into existence about 250 million years ago, the continents were part of one massive supercontinent called Pangaea. Dinosaurs went extinct about 65 million years ago, and our ancestors, the prosimians, emerged about 63 million years ago. At about this time, the continents of Asia, Africa, Europe, North and South America, and Australia took on the form that we know today. The theory of plate tectonics, developed in the 1950s, made it clear that mountainous regions such as the Himalayas came into being over the course of tens of millions of years. The photograph shows a rock found in the Himalayas. A fossil of a shell can be seen in the rock, providing evidence that in the ancient times, the Himalayas were under the ocean.

When mammals replaced dinosaurs as the rulers of Earth about 65 million years ago, the concentrations of oxygen and carbon dioxide in the atmosphere and sea were completely different from what they are now. We earlier posed the question of how migrating birds flying over the Himalayan peaks at ease have adapted to hypoxia. Although the current atmosphere is 21% oxygen, it was only 15% when birds evolved. Thus, the ancestors of birds likely evolved to adapt sufficiently to hypoxic conditions.

The biosphere also faced the challenge of changing temperatures. Glacial periods are relatively rare in history, with three such periods that occurred about 400 million years ago, 275 million years ago, and 2.5 million years ago. In midst of the cycling temperature changes, there were also periods of extreme changes in heat. This is evidenced by the existence of insects, such as the wooly aphid that lives in glaciers, as well as microbes that live in hot springs, sulfur vents, volcanos, and undersea hydrothermal vents at temperatures as high as 120° F.

As discussed above, dramatic physical changes occurred in the global environment during Earth's 4.6 billion year history, and the biosphere constantly adapted to these changes and evolved.

Biosphere-anthroposphere interactions

Although humans are an integral part of the biosphere, a specific relationship exists between food and illness when considering biosphere-anthroposphere interactions.

With the mass extinction of dinosaurs about 65 million years ago came the dawn of mammals. Having lived nocturnally as small animals until then, mammals came out in the open during the day. The accidental extinction of dinosaurs allowed these mammals to take over as main actors. This KT boundary served as a junction for mammals. Our ancestors, the prosimians, evolved from these mammals and eventually branched off into anthropoids, a subset of which evolved into humans. Although early mankind was high up on the food chain, they were not at the apex. For a few million years after mankind's ancestors came into existence, they had no choice but to co-exist with large carnivores that also preyed on human species in the African savanna. One can say that when mankind was hunting and gathering in the early stages of the anthroposphere, humans were still an integral part of the global food chain and abided by nature's laws.

The agricultural revolution brought about a breakthrough in human diet about 10,000 years ago. At this time, mankind learned to domesticate wild plants and animals and invented farming. Agriculture made increased food production and storage possible. Those not engaged in agriculture became soldiers, bureaucrats, and technicians, further spurring the evolution of society. At the same time, this brought about social and gender inequalities. The increase in human diversity and divide between tribes arose in the past 10,000 years or so.

Agriculture not only brought about groundbreaking advances in the anthroposphere, but also presented new threats to the foundation of human survival. While it was likely difficult to secure daily meals when humans were hunting and gathering, they were nonetheless able to maintain adequate variety in meals from the perspective of protein, mineral, and vitamin intake. With the advent of agriculture, however, the main energy source shifted to carbohydrates, leading to the biased intake of nutrients and increase in malnutrition. When comparing nutritional intake between hunters and gatherers and farmers, paleopathology reveals that hunters and gatherers likely led a healthier lifestyle.

Agriculture relies on a limited number of crops. As a result, in addition to nutritional balance issues, poor harvest years brought about famine due to difficulties in securing sufficient food to feed groups with large populations. Since the agricultural revolution, the threats of malnutrition and famine increased substantially more than experienced during the period of hunting and gathering.

Disease epidemics, the greatest misfortune in human history, form a byproduct of the agricultural revolution. Although increased food production made denser populations possible, it also brought about epidemics. Infectious diseases were rampant among highly populated, malnourished groups, and were transmitted from animal to humans and from human to human. Epidemics resulting from the concentration of populations were not a problem for hunters and gatherers, who kept in small-sized groups and constantly traveled. The emergence of bacterial infectious diseases that transmit from human to human, such as tuberculosis, leprosy, and cholera, became particularly pronounced after the advent of agriculture. Viral infections such as smallpox, the bubonic plague, and measles are thought to have arisen in the past several thousands of years since cities began to form and concentrated populations became possible. Since the beginning of agriculture until recent times, about one-fifth of the human population is estimated to have died before the age of 5 years due to infectious diseases or malnutrition during infancy. Even now, an arms race ensues between the biosphere (pathogenic microbes) and anthroposphere in the form of the development of new antibiotics and evolution of drug-resistant microbes.

Anthroposphere-anthroposphere interactions

Struggles within the anthroposphere, i.e., wars, represent a phenomenon that became pronounced after the advent of agriculture. Several human species are thought to have existed about 200,000 years ago.

While human species we know of today, such as *Australopithecus, Homo habilis, Homo erectus,* and Neanderthals, were all fated to extinction, no conclusive evidence exists that they fought each other.

While many human species remained in Africa, some moved to Eurasia about 1.8 million years ago. This is known as the first migration from Africa. These species, later to become known as the Peking man and Java man, are referred to as *Homo erectus*, along with their fellow species that remained in Africa. At least one group of *Homo erectus* began using fire, a monumental event in mankind's history. Homo erectus survived until 250,000 years ago.

The era of modern humans began about 200,000 years ago. This era is notable as the period during which symbols, such as language, and original forms of artistic expression, came into use. Coexisting with modern humans were the Neanderthals. In an event known as the second migration from Africa, one group of modern humans left Africa about 100,000 years ago and eventually adapted to all environments in the world. Mankind conquered various terrains, including grasslands, deserts, and mountains, and began living in various climates (tropical, temperate, and polar). They advanced into every environment, as exemplified by the Eskimos in polar regions, bushmen in the deserts, pygmies living deep in the rainforests, and Tibetans living in highlands. The speed of this expansion is particularly striking, as within tens of thousands of years, humans reached Europe, Asia, South and North America, and Australia.

This migration of early stage humans was likely prompted by a desire to avoid fighting over limited resources and search for a frontier that would serve as a new niche. However, the situation began to deteriorate after the agricultural revolution. Agriculture brought about repeated conflicts over limited land, resources and labor forces. This further exacerbated the stratification of social structure, as exemplified by the divide between people with power, aristocracy, soldiers, and farmers. The history of mankind, who began writing about the past in words, is rife with descriptions of war.

Up until 50 years ago when global environmental issues were laid out on the table as a topic for discussion among international society, humans, over the several thousands of years of their history, were engaged in an arms race linked to the destruction of the global environment. Even in current times, armed conflicts transform into fights over rights of possession of resources, economies, and information-no harmonious solution has been achieved on this front. Even when taking up the one issue of preserving the global environment, there is no hope for a quick solution or consensus, as developing and developed countries have their different interests and views. Indeed, global environmental issues are anthroposphere-anthroposphere-based social problems.

History of the "Global Environmental Disaster (GED)"

When considering global environmental issues, a broad, entangled, and multilayered phenomenon interpreted differently by region, it helps to view the historical shift of the subject at hand. It is possible to tentatively name the changes brought about by stresses to the environment as a result of human production and consumption activity since the 20^{th} century (e.g., pollution, global warming, water pollution, reduced rainforests, and desertification) as the "Global Environmental Disaster (GED)." Rather than the narrow sense of global environmental issues currently faced by mankind, this broadens our perspective to the enormous changes brought about by geosphere-biosphere-anthroposphere interactions, and makes clear that many GEDs have occurred over the course of Earth's history. It is most typical to approach questions about interactions between Earth, life, and humans, and the direction these interactions are headed, by exploring case histories.

Oxygen concentration in the atmosphere

Hypoxia is an absolute reality of highland environments. While the fact that the atmosphere consists of 21% oxygen does not change, given that atmospheric pressure is reduced in highlands, the concentration of oxygen in the atmosphere at an altitude of 5000 meters is one half that at sea level, and it becomes one third at an altitude of 8000 meters.

While we fear changes in the global environment, this is premised on our inclination to think that the world that we comfortably live in has existed in its current form for ages. We are prone to think that the oceans, mountains, and even the composition of air in the atmosphere are eternal. Until the theory of plate tectonics was developed in the latter half of the 20th century, Earth's continents were thought to have been fixed in their current position. This mistaken mindset is evident more so with respect to oxygen, which is required for life, as we are inclined to think that its levels have been maintained for ages.

According to Peter Ward, even 5 million years ago, which is only a brief moment on the geological time scale, the concentration of atmospheric oxygen may have been higher than current levels, while 60 million years ago, the concentration was clearly lower.

The planet known as Earth came into existence about 4.6 billion years ago in what we know as the Big Bang. With the expansion of the universe came hydrogen and helium, followed by the birth of stars and the formation of metals within the stars. The Earth was formed through the constant collision of dust and mineral particles orbiting the sun, and at the time of its birth was molten due to the flurry of collisions. Elements forming the dust particles of Earth mixed, and recombined to form new minerals. While there was essentially no oxygen in the atmosphere at the dawn of Earth, atmospheric carbon dioxide was more than 10,000-fold higher than current levels, and this is thought to have led to an extreme greenhouse effect. From at least 3.5 billion years ago, cyanobacteria, which use sunlight for photosynthesis, arose and began producing oxygen. A group of cyanobacteria transitioned to plant cells and became chloroplasts. Through extensive photosynthesis, they contributed to the accumulation of oxygen in the atmosphere. However, until 2.2 billion years ago, the concentration of oxygen in the atmosphere is thought to have been, at most, 2-3%.

According to the GEOCARBSULF model, which estimates the concentration of oxygen and carbon dioxide in the atmosphere of past geologic periods, the concentration of oxygen in the Cambrian age (about 550 million years ago), which was notable for the explosion of new species of life, was substantially lower than the present 21%, at about 15%. However, the ensuing 200 million years saw the concentration increase from 15% to 25%. About 380 million years ago, the concentration went back down to about 15%, but then again increased about 260 million years ago to the maximum value of near 30%. At around the beginning of the Jurassic period of the Mesozoic era (about 190 million years ago), the concentration of oxygen decreased below 15% to a record low, and since then, while vacillating up and down, reached the current 21%. It has also become apparent that the concentration of carbon dioxide and oxygen were inversely proportional, and this relationship differed by geologic period. As we know today, the concentration of carbon dioxide in the atmosphere influences Earth's temperature through the greenhouse effect, contributing to the formation of characteristic climates throughout the course of Earth's history.

Changes in the concentration of atmospheric carbon dioxide and oxygen are thought to have had an important and deep impact on the anthroposphere and its evolution. This is believed to have been involved in the mass extinction of life discussed below.

Mass extinction of life

The history of life is ridden with a sporadic, rapid series of mass extinctions. About 10 such extinction events have taken place within the last 500 million years, the most well-known of which are discussed below.

At the end of the Proterozoic era (Pre-Cambrian period), about 600 million years ago, soft-bodied organisms known as the Ediacara biota were prominent. They disappeared about 545 million years ago in what is known as the VC boundary (the first extinction). After their extinction, trilobites flourished, but a mass extinction that occurred during the Ordovician period of the Paleozoic era (about 435 million years ago) reduced the number of trilobite species by half. Trilobites were not the only victims, as about 85% of all living species are thought to have gone extinct. At the end of the Devonian period of the Paleozoic era (about 360 million years ago), placoderms, such as Dunkleosteus, and many marine organisms, such as armored fish, went extinct, as did about 82% of all living species.

During the Permian period at the end of the Paleozoic era (about 225 million years ago), the largest mass extinction known to date occurred, which is referred to as the PT boundary. Victims included all trilobites, all ancient corals, all ammonites with the exception of one strain, and most bryozoans, brachiopods, and crinoids. This mass extinction also saw the death of many synapsids (i.e., mammal-like reptiles) that flourished during the Paleozoic era. Among the archosaurs that survived this period and flourished in the Triassic period were dinosaurs that first adapted to the hypoxic environment by acquiring air sacs-these species formed the foundation for the following period of prosperity. Synapsids that developed diaphragms and acquired the ability of abdominal breathing also overcame the threat of the hypoxia to become the ancestors of mammals. Following the PT boundary, during the late Triassic period of the Mesozoic era (about 212 million years ago), many ammonite species, along with the lineage of many large reptiles and synapsids, were among the 76% of all living species that succumbed to mass extinction. This period saw the rapid expansion of dinosaurs, which at the time were relatively small in size.

Dinosaurs flourished from the late Triassic period to the Jurassic-Cretaceous period, but suddenly went extinct about 65 million years ago. This extinction event, which places second in scope in the evolutionary history of organisms, is known as the KT boundary. While many views exist, the leading view has it that the mass extinction was caused by an asteroid colliding with Earth near the Yucatan peninsula. The resulting fire and dust that blocked sunlight led to globally-reduced temperatures, paving the way to mass extinction. About 25% of living species went extinct, effectively cleaning out the dinosaurs which ruled the land up to that point. This was an important turning point for mammals, and the event that set the stage for human evolution.

The events discussed above are known as the "five mass extinctions," and a common factor shared by four of these is hypoxia. During the Ordovician, Devonian, and Triassic periods, the concentration of oxygen in the atmosphere decreased to below 15%, whereas the concentration decreased by 10% when the Permian mass extinction occurred. While these mass extinctions are events in geological history, some biologists take the view that a mass extinction is currently underway. For instance, Wilson estimates that mankind's destruction of the biosphere will kill off half of all species on Earth within 100 years.

History of mankind

Mankind is thought to have split from common ancestors with chimpanzees about 7 million years ago. At the time, the habitat of Africa's forests began to undergo desertification, leading one group to leave the treetops for the savanna. Many early stage human species are known to have walked erect, and walking erect was likely attempted many times by numerous groups. While many theories attempt to explain why mankind transitioned from walking on all fours to walking erect, this remains an unsettled question. Bipedalism clearly conferred the ability to carry food in hands, made it possible to see further distances, and eventually led to an expansion in brain volume. It took 4 million more years from the time our ancestors began walking erect for our brain volume to expand. One explanation for this evolutionary delay is climate change in Africa. The progressive drying of the climate led to a reduction of forests, and our ancestors living in the grasslands were subjected to a natural selection pressure unlike any known before-this is thought to have led to changes in body structure and behavior. One reason why orangutans, which were transported to Asia by continental drift, remained in the trees is probably because the rich forests in Asia's tropics were preserved about 2.5 million-30 million years ago, while the northern hemisphere and Africa progressively became cooler and dryer.

The development of glaciers about 2.5 million years ago and the resulting drastic change in climate likely instilled a potent selection pressure on the several thousand species living on Earth. This pressure prompted adaptations to the new conditions in order to facilitate specific organisms' success in propagation. Evidence exists for enlarged brains and the use of tools from about 2.5 million years ago. The concept of preadaptation in evolutionary biology refers to gradually changing body structure so that, when a particular environment is faced, the changes work to one's advantage. The advantages of bipedalism are thought to have played an important role in human evolution again 2.5 million years later. Armed with an expanded brain volume, mankind began using stone tools and brought about a revolution in food energy-the intake of high calorie meat rich in nutrition. Despite being "meat-eating" and hunting herbivorous animals on occasion, most of the food supply likely came from rotten meat left over by carnivorous animals. The expansion of brain volume led to improvements in meat eating efficiency, and was accompanied by acquiring the body structure of modern humans, increases in range of activity, and loss of body hair.

The genetic design acquired by mankind over 7 million years of evolution was designed to adapt to the African environment. When considering the entire span of human evolution, the achievement of bipedalism was a groundbreaking event. In order for bipedalism to be possible, it was necessary to undergo morphological changes to the pelvis and develop complex motor skills for body balance. Even from the standpoint of human ontogeny, achieving stable body balance takes infants many years. The stability of bipedalism, once achieved, declines later in life with advancing age. Genes probably did not foresee that, 7 million years later, bipedalism would cause falls and fractures, which are ranked third for reasons elderly are bedridden. Abilities that worked to one's advantage in youth have the opposite effect in old age, i.e., a biological trade-off. Bipedalism is considered a typical case of such a trade-off. From the perspective of evolutionary medicine, parallels are also seen between the evolution of intelligence resulting from the enlargement of the brain, and Alzheimer's disease in old age.

Mankind has continuously altered the global environment since the agricultural revolution. They increased the density of populations while living settled lives, but some also sought new farmlands or grazing lands, and developed livelihoods in all environments throughout the world. By taking advantage of a region's particular nature/ecosystem, humans developed cities, established trade networks between regions, created a human-specific social mechanism called "civilization," and even began to contemplate the well-being of their spiritual world.

The highlands, which served as the site for the Highland Project, are an example of such a frontier.

Research paradigm for global environmental issues

Thought experiment

The "global environment" can be considered a massive, complex system that takes sunlight as its source of energy in order to weave a grand tapestry of biochemical, biological, geological, economical, and political energy exchange.

Kauffman, a researcher of complex systems and the theory of evolution, states that "one way to underline our current ignorance is to ask, if evolution were to recur from the Precambrian when early eukaryotic cells had already been formed, what organisms in one or two billion years might be like." The main shortcoming of our current view of evolution is that it never led us to ask such questions, despite the fact that the answer may provide us with deep insight into the qualities that organisms are expected to develop.

Until the early 20th century, scientists believed that climate and the chemical composition of the atmosphere were fixed and a given. We now know that organisms were responsible for conditioning the atmosphere to have a particularly high oxygen and low carbon content. One view has it that atmospheric changes occurred under the influence of biological evolution. Life influences climate, at times, to the extent of influencing glacial periods and droughts.

Through Kauffman's thought experiment, one can confirm the products of nature's experiment with mammalian evolution over the long 65 million year period since the extinction of dinosaurs, for example, in lemurs in Madagascar, a region isolated from the rest of the world, ungulates of Australia, and even in places where mammals never existed, such as New Zealand. The continents had been shifting. Ancestors of new world monkeys, born in Africa, were carried, like lemurs, on continents to the Americas, and can be now found in both Central and South America.

Lenski experimentally validated Kauffman's views in a laboratory setting. About 10^{20} *Escherichia coli* exist in the world, and a human has about 1 billion *E. coli* in the large intestine. Over the course of 20 years, Lenski and colleagues serially passaged 12 populations of E. coli that divide every 20 minutes. After about 40,000 generations, they performed an evolutionary experiment by introducing a period of abundant nutrition followed by starvation. The results of this experiment can be used to explain why, no matter how fast new antibiotics are developed, microbes instantaneously acquire a resistance to them. This led to the view that, from an experimental perspective and based on results of evolutionary experiments, the strategy of developing new antibiotics is not the right approach.

In the context of infectious diseases, there are limits to engineered disinfecting methods. Indeed, the need for an evolutionary medicine-based approach is evident. One such strategy is to 'coexist with microbes.' That is, even if infected, an approach that delays the onset of disease or symptoms as much as possible-past the human lifespan, for example.

"If" is a taboo word in history. At the same time, we regularly use expressions like "history repeats itself," "the present-day significance of historical research lies in viewing and designing the future," and "the lessons of history apply to the future." In such cases, the historical "if" represents an important thought experiment.

When considering global environmental issues, a vast, evolutionary history-based thought experiment might offer the key. From the standpoint of a "thought experiment," the interpretation of history lends itself to various opinions that are not necessarily aligned along a single path. This process becomes possible only when mobilizing sciences, such as ecology, meteorology, geophysics, paleontology, and medicine, in addition to humanities-like historical studies that rely on documentary records.

Infectious diseases and the global environment

The landmark discovery of cholera by Koch at the end of the 19th century elegantly proved the hypothesis that diseases can be traced to single factors, such as viruses and bacteria. Following this, it was also discovered that mold, toxins, and vitamin deficiency can lead to illnesses. This established the model in medicine that one pathogen leads to one disease. This model contributed to the prevention of various diseases by avoiding, killing, or acquiring a resistance to specific bacteria and viruses.

From the 19th century to the first half of the 20th century, deaths due to infectious diseases markedly decreased. Public health methods based on the one pathogen-one disease model effectively severed the path to infection by specific bacteria. In 1910, Paul Elrich and Sahachiro Hata discovered the drug salvarsan which targeted syphilis, and in 1928, Fleming discovered penicillin. Since then, an enormous variety of antibiotics have been developed, allowing mankind to conquer most infectious diseases, which led in turn to the extension of lifespan. Human waste was completely removed from the water supply, and continuous efforts were made to remove pathogens from the food supply. By implementing vaccinations, developing drugs to treat diseases, and blocking the path of bacterial infection, it appeared that infectious diseases, for the most part, were eliminated.

A large number of antibiotics were developed since then, and it appeared that mankind had eradicated infectious diseases for good. In 1969, the U.S. Surgeon General William Stewart reported to Congress that it was time for developed countries to "close the book on infectious diseases." Yet, by the 1960s, methicillin-resistant *Staphylococcus aureus* was discovered, marking the rise of new and re-emerging infectious diseases.

The traditional strategy of attempting to eradicate pathogenic bacteria with pharmacological methods, such as antibiotics, only serves as a temporary solution. More basically, for example, there are currently searches for strategies of co-existing with these pathogens, while delaying the onset of diseases/ symptoms to past a human's lifespan.

The spread of infectious diseases can be classified in the order of smallest to largest scale as follows: endemic (regional), epidemic (national and involving several countries), and pandemic (global). Global environmental issues, too, are initially considered endemic problems arising in various regions that threaten residents and crops. These eventually come to be considered in terms of common factors (epidemic) shared by problems across multiple regions, and when these problems go global (pandemic), they are considered "global environmental issues." The causes of global environmental issues are complex, and likely involve various factors. However, the issues initially take on a concrete form in "regions," and how the issues come to light likely differs by the mode of life or culture of the region. By combining science, which takes a universal approach in surveying the global environment, and regional research, which is well-acquainted with the workings of individual regions, the nature of global environmental issues becomes all the more apparent. When considering preventative measures to take against global environmental issues based on scientific predictions, it is necessary to carry them out in a way that comports with the current condition of the region.

Population increases, extension of lifespan, and lifestyle-related diseases

It is essentially a given that the actions of humans and the increase in global population are causes of global environmental issues.

Through the last stages of the hunting and gathering period, mankind formed groups of tens of people and repeatedly traveled as hunters and gatherers. The global population is thought to have been 100,000 about 1 million years ago, and grew to about 500,000 roughly 200,000 years ago when modern humans were born, and then to about 10 million when agriculture began about 10,000 years ago. After that, the population continued to increase, although it was less than 1 billion before the Industrial Revolution. It thus appeared that a delicate balance was stuck between the global population and environment. Only since entering the 20th century, more specifically the past 50 years or so, have global fears presented in the form of global environmental issues come to light. The 100 years of the 20th century were marked by technological breakthroughs, changes in disease structure, globalization of politics and economics, and last, but not least, an increase in global population. This last factor deserves special mention from the perspective of mankind's history. The global population within these 100 years may in fact be larger than the total number of humans that existed from mankind's birth 7 million years ago to the 19th century.

The 20th century is not only the century of huge population growth, but it is also the century of extended human lifespan. While concentrated populations began to form about 10,000 years ago with the advent of agriculture, human lifespan was largely unchanged. However, the latter half of the 20th century brought about phenomenal changes in mankind's 7 million year history. An extended lifespan, which was one such change, brought about marked changes in population structure.

Even in the highlands, average lifespan increased as the food supply stabilized, and relief from starvation is now giving way to satiation. Fat, sugar, and salt were essentially lacking in all of highland history. Most people, who lived for about 30-40 years, took as much of these substances as possible, thinking it healthy, and adapted to the environment.

However, the plentiful intake of salt, which only recently became possible, leads to hypertension and stroke once past the age of 40 or so. Bodily mechanisms for storing energy, which were meant for times of starvation, lead to diabetes due to a satiating diet. The cholesterol metabolism pathway, a system of storing fat and effectively utilizing it in times of food shortage, causes cholesterol to deposit in blood vessel walls once past the age of 40, leading to arteriosclerosis and myocardial infarction.