General and Comparative Endocrinology 186 (2013) 145–149

Contents lists available at SciVerse ScienceDirect

General and Comparative Endocrinology

journal homepage: www.elsevier.com/locate/ygcen

Minireview

Evolutionary medicine and its implications for endocrinological issues (e.g. menopause)

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ARTICLE INFO

Article history:
Received 24 January 2013
Accepted 21 February 2013
Available online 20 March 2013

Keywords:
Darwinian medicine
Evolutionary medicine
Endocrinology
Female reproductive senescence
Menopause
Climacteric symptoms

ABSTRACT

Evolutionary medicine, which was formalized in the early 1990s, investigates evolutionary causes of recent human disease, disorders and malfunctions but also the influence of changing living conditions and modernization on health and disease. Evolutionary medicine can also provide insights into endocrinological disorders and in particular in the process of female reproductive senescence. Female reproductive senescence, i.e. menopausal transition is physiologically caused by the decline of estrogen secretion, which is associated with various somatic and psychic discomforts making this stage of life extremely uncomfortable. From the viewpoint of evolutionary medicine, these menopausal symptoms are the result from the sudden decrease of very high lifetime estrogen levels to zero during postmenopause, a situation which is quite new in our evolution and history. While women in recent developed countries experience menarche early, menopause late, few pregnancies, short periods of lactation and consequently low life time estrogen levels. The opposite is true of women living in traditional societies, whose living conditions may be interpreted as a mirror of the situation in our history. From this viewpoint we can conclude that menopausal symptoms may are the result of a mismatch between female reproductive physiology and recent living conditions.

1. Introduction: origin and aim of evolutionary medicine

According to Dobzhansky (1973), "*Nothing in biology makes sense except in the light of evolution*". Therefore, beside proximate factors ultimate explanations for each condition are necessary (Voland, 1993). This shall be particularly true for medical conditions eventually allowing a better understanding of current health care issues. More than 150 years after the publication of Charles Darwin's fundamental work "On the Origin of Species by Means of Natural Selection" in 1859 (Darwin, 1959) and 140 years after publication of his second important publication "The Descent of Man and Selection in Relation to Sex" in 1871 (Darwin, 1871), evolutionary theory is not only a unquestionable part of natural science, a Darwinian approach is thus getting more and more established in medical science too. Evolutionary theory is without any doubt associated with the name of Charles Darwin (1809–1882), who not only introduced the terms biological evolution, natural and sexual selection in science, but also considered evolutionary explanations for behavior and disease. Soon after his death in 1882, a group of physicians tried to construct a Darwinian theory of disease, but these early ideas had nothing to do with the principles of evolutionary medicine today. The term "Darwinian medicine" was introduced by Benjamin Ward Richardson in 1893; however, he was speaking about the medicine of Erasmus Darwin the grandfather of Charles Darwin (Zampieri, 2009). Darwinian or better evolutionary medicine in a recent sense was formalized in the early 1990s most notably by the evolutionary biologists George C. Williams and psychiatrist Randolph Nesse (Williams and Nesse, 1991); at least three main monographs have initiated evolutionary medicine (Nesse and Williams, 1994; Stearns, 1999; Trevathan et al., 1999).

At first, Williams and Nesse tried to understand why natural selection has left the human body so vulnerable to diseases (Williams and Nesse, 1991). According to their concept, many medical conditions that are clearly pathological today have been adaptive in the ancestral environment in which Homo sapiens evolved and thus have been selected positively for. Consequently, the science of evolutionary medicine is concerned with identifying and understanding these conditions. It is thought that evolutionary perspectives on disease and individual symptoms can elucidate pathophysiology and ultimately inform treatment strategy. The concept of evolutionary medicine was born (Nesse and Williams, 1994).

During the last 20 years after Williams and Nesse's initial publication, the concept and applications of evolutionary medicine

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http://dx.doi.org/10.1016/j.ygcen.2013.02.046

experienced their own evolution. Today the aim of evolutionary medicine is to investigate evolutionary causes for human disease, disorders, malfunctions and design failures in order to improve health of recent populations. Additionally the history of diseases is focused on in order to understand how changing living conditions but also processes of modernization and acculturation influenced health and disease. Evolutionary medicine shall also focus on ongoing molecular (and morphological) alterations, both of humans but also of pathogens (Fuller, 2011; Lozano, 2010; Nesse and Stearns, 2008).

To clarify what evolutionary causes of diseases are, we have to start with an explanation of the different levels of causality in biology. In general, we have to distinguish between proximate and ultimate or evolutionary explanations of biological phenomena (Voland, 1993) Proximate causes are immediate mechanisms such as physiological or fetal and embryologic factors, of disease, disorders or malfunctions. Ultimate explanations, in contrast, tried find the reasons of recent diseases in our history or evolutionary past (Harris and Malyango, 2005; Voland, 1993).

Summarizing, according to the concept of evolutionary medicine many medical conditions that are clearly pathological today have been adaptive in the ancestral environment, the so-called environment of evolutionary adaptedness, in which *H. sapiens* evolved. First of all, evolutionary medicine has provided insights into the origins of non-communicable diseases, such as metabolic diseases, diabetes and obesity typical for the second half of the twentieth century and the beginning 21st century (Trevathan, 2007). Additionally evolutionary medicine has also attempted to explain the origin of certain problems associated with female reproductive function such as complications during childbirth, amenorrhea but also menopause (Rosenberg and Trevathan, 2002; Strassmann, 1999; Trevathan, 2007). The aim of this mini-review is to specifically address exemplary such issues where evolutionary medicine can provide insights into endocrinological disorders and conditions. Exemplary, female reproductive senescence will be addressed.

2. The evolution of *Homo*: environment of evolutionary adaptedness

Members of the genus *Homo* are characterized by an obligatory bipedal locomotion and marked changes in social behavior and dieting habits. Increased brain size and larger body size made increased energy supply essential. This increased demands of energy to meet the metabolic costs of the energy expensive brain resulted in numerous anatomical as well as behavioral adaptation (Aiello and Wells, 2002). On the one hand, the size of the energy-expensive gut was reduced and nutritional habits changed toward and increased meat and fat consumption (Aiello and Wheeler, 1995). About 100,000 years ago, modern *H. sapiens* originated in Africa and colonized with the exception of Antarctica the whole world. Up to now, it is not completely clear, whether modern *H. sapiens* has replaced earlier hominin occupants or modern *H. sapiens* may have interbred with them (Henke and Hardt, 2011). Modern *H. sapiens* has adapted to widely different habitats and showed a huge developmental plasticity to survive and reproduce successfully under widely different environmental circumstances.

The environment experienced by members of the genus *Homo* and by *H. sapiens* has been called the environment of evolutionary adaptedness (EEA) (Bowlby, 1969). This environment was characterized by a foraging subsistence based on hunting and gathering, the use of stone and wooden tools, a mobile (nomadic) life style, small multi-aged egalitarian groups consisting of 20–30 group members. There was a lack of domesticated animals with the exception of the dog. Ethnographic analyses of the few remaining contemporary forager populations such as the Hadza in Tanzania, the !Kung of Namibia and Botswana, Ache of Paraguay or Efe of central Africa provided information about diet and life style in a foraging economy (Howell, 2010; Marlowe, 2010). It is well documented that diets consist to a high degree of vegetable food, protein (50–80%) and a low fat content (Bogin, 1997; Cordain et al., 2002; Eaton et al., 1988; Eaton and Konner, 1985; Hockett and Haws, 2003; Kious, 2002; Konner and Eaton, 2010). The typical life style is highly mobile because high levels in daily activity in search of food, water and sleeping sites are necessary. From a medical point of view typical non-communicable diseases such as hypertension, heart disease, cancer, diabetes or obesity are rather unknown (Cordain et al., 2002; Lieberman, 2003). *H. sapiens* is clearly adapted to an environment like this.

About 20,000 years ago the process of Neolithic transition started resulting in the emergence of agriculture and a complete change in subsistence economy and life circumstances about 10,000 years ago in the area of the fertile crescent (Maher et al., 2012; Rosen and Rivera-Collazo, 2012). Neolithic transition changed human lifestyle dramatically (Armelagos et al., 1991; Larsen, 1995). Domestication of animals and plants allowed the production of a surplus of food. Consequently humans developed semi-permanent settlements and gave up their mobile lifestyle. The production of food allowed a considerable population growth because more people could be supported on the food grown. On the other hand, the adoption of agriculture and animal husbandry led to dramatic dietary changes. Dietary breadth was reduced dramatically and diet consisted of high carbohydrate crops such as rice, barley or wheat and tuber such as potatoes (Larsen, 1995; Mann, 2004). Analyses of Neolithic skeletal remains indicate protein deficiencies and periodic food shortages, skeletal conditions which can clearly be interpreted as results of famine and starvation. Furthermore, domestication of animals and plants changed the environments dramatically. The use of feces as fertilizer and the construction of irrigation increased the contact with parasites. Additionally the close proximity to domesticated animals exposed humans to a variety of new pathogens resulting in an increased frequency of infectious diseases (Armelagos et al., 1991). Therefore, Neolithic transition has led to the so-called first epidemiologic transition (Barrett et al., 1998; Omran, 1971; Omran, 1983). A second epidemiologic transition occurred about 200 years ago during Industrial Revolution when a shift towards manmade diseases is observable.

3. Issues of recent environment

During the 20th and 21st century, the third epidemiologic transition occurred, characterized by a decline in infectious diseases and a rise of non-communicable and degenerative diseases often as a consequence of increased life expectancy (Armelagos et al., 1991; Barrett et al., 1998). We have to be aware that our recent environment is completely different from that in which our species evolved. An increasing number of people live in urban environments, many of them in so-called mega cities of more than 10 million inhabitants. Recent urban *H. sapiens* live alone or in small nuclear families in a quite anonymous society. Technical advances and modernization of lifestyle resulted in a marked transition in human life style. Exemplary, medical interventions and practices change remarkable human morbidity and mortality. The opportunity for natural selection through differential mortality thus has changed remarkably. Also, daily energy effort to gather and prepare enough food is reduced nearly to zero, since only few individuals are working in food production. Mechanized transportation, sedentary jobs and labor-saving household technologies reduce physical activity too. On the other hand, more than enough energy dense food, mainly consisting of sugar and fat is easily available