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To cite this version:

Sylvie Odent, Michel Odent. Primal health research in the age of epigenetic clocks. Medical Hypotheses, 2019, 133, pp.109403. 10.1016/j.mehy.2019.109403 . hal-02304763

HAL Id: hal-02304763

https://univ-rennes.hal.science/hal-02304763v1

Submitted on 7 Jul 2020

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Medical Hypotheses 133 (2019) 109403

Contents lists available at ScienceDirect

Medical Hypotheses

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

Primal health research in the age of epigenetic clocks

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ABSTRACT

In the field of developmental origins of health and diseases among humans, classical epidemiology has limited power. We hypothesize that widely available "biological clocks" would introduce a new era in the history of health research.

By contrasting chronological age and physiological age, "biological clocks" might become instrumental, without any delay, in exploring the possible long-term effects of a highly modified lifestyle during the "primal period". The aging process, life expectancy and health in general would be the main criteria. Today "DNA methylation GrimAge", based on estimations of plasma protein levels, may be considered to be the best predictor of lifespan and healthspan.

Since the publication of the book "Primal Health", in 1986, we have been collecting published epidemiological studies that explore correlations between "the primal period" and what happens later on in life in terms of health and personality traits (www.primalhealthresearch.com) [1]. The "primal period" starts at conception and is over around the first birthday. It may be presented as the phase of life when our basic adaptive systems – those involved in what we commonly call health – are reaching a high degree of maturity.

In the age of classical epidemiology

Our database has fulfilled several roles. At a time when, for obvious reasons, human beings have been suddenly "condemned" to dramatically develop their long-term thinking, the database may be first presented as a training tool in terms of prospective capabilities. This function will probably be reinforced, in the near future, through an increased number of studies related to the keyword "transgenerational". Since many of the studies we have collected are based on huge numbers, with results expressed in statistical language, the database is also instrumental in enlarging another aspect of our way of thinking: until recently, health professionals and the general public were constantly misled by the transmission of purely anecdotal observations by authoritative individuals.

Correlations provided by primal health research are never self-sufficient. Interpretations rely on the use of criteria, such as the bradford hill criteria.

The sudden fast development of disciplines with a strong explanatory power, such as epigenetics, metagenomic bacteriology and endocrinology leads to a renewed understanding of the criterion "plausibility".

Today, the point is to realise the limits of classical epidemiology. There are spectacular transformations, at a global scale, in the lifestyle of modern humans during the primal period. Primal Health Research is not yet based on what the priorities should be: it is becoming imperative to phrase new questions about the possible long-term non-specific effects on health of present-day routine interferences, particularly in the framework of medical care. We must transcend the conventional questions focusing on the short-term ratios of benefits to risks of human actions.

Evaluating the age-related physiological decline

Fifty years ago, nobody could anticipate the time when nearly all human beings would be exposed to specific ultra sound frequencies during the phase of foetal development, when nearly all human beings would be exposed to synthetic oxytocin before a vaginal or a caesarean birth [2], and when nearly all human beings would receive a great number of vaccinations during their primal period.

Today the point is not to express opinions and theories. It is to explore the possible long-term effects of a renewed lifestyle during the primal period on criteria such as the aging process, life expectancy and health in general. For technical and ethical reasons, the "golden method" in epidemiology is rarely available. One cannot, at random, deprive thousands of human beings of the information provided by ultrasound explorations, of the help provided by synthetic oxytocin during the birth process, and of the protection provided by vaccinations during pregnancy and early infancy. Furthermore, one cannot wait until the 22nd century to analyse valuable data provided by conventional

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https://doi.org/10.1016/j.mehy.2019.109403
Received 1 August 2019; Received in revised form 7 September 2019; Accepted 18 September 2019
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prospective studies.

In such a context, the concept of a biological clock is of great interest. In the near future we'll undoubtedly have at our disposal possible ways to contrast the chronological age, based on the date of birth, and multiple aspects of the physiological age. From now on, one can take advantage of new ways to explore, on an individual scale, the aging process and to evaluate the state of health and the life expectancy.

The first example of a valuable biological clock was based on the work of Elizabeth Blackburn, Carol Greider and Jack Szostak on telomeres (they were awarded the Nobel Prize in Physiology and Medicine in 2009). They had discovered that telomeres – protective caps on the ends of chromosomes – shorten with age. Measuring telomere length is theoretically a way to evaluate the functions of immune stem cells.

Today it seems that the most promising kind of biological clock is related to the fast development of epigenetics, this emerging discipline based on the concept of gene expression. As early as 2011, the team of Steve Horvath, in Los Angeles, provided the first robust demonstration that DNA methylation in saliva could generate accurate age predictors. [3] Let us recall that DNA methylation is a commonly used epigenetic signalling tool that can fix genes in the "off" position. It undoubtedly plays a key role in the aging process, health maintenance, carcinogenesis, the genesis of the metabolic syndrome, and the recovery from pathological condition. Some periods of human development seem to be critical in terms of epigenetic activity.

In January 2019, a new step was reached when it was revealed that "DNA methylation GrimAge", as an epigenetic clock based on estimations of plasma protein levels, can strongly predicts lifespan and healthspan. [4] Now researchers have at their disposal a biological clock which is impressive with its accuracy and prides new reasons to focus on the concept of timing. This might open the door to a new phase in the history of Health Research.

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