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Commentary Article

Humans Have Metabolism Systems of Glucose and Ketone Bodies

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Abstract

From the biological point of view, humans have undergone various evolutions for long. Humans and monkeys are belonged to the primate species, which have neuroendocrine system (NES) with an important role in controlling several axes for regulating the growth, stress, metabolism and reproduction. There are important metabolic systems of glucose and also ketone bodies (KB) which can produce much energies. Recent topics for nutrition therapy include the comparison of calorie restriction (CR) and low carbohydrate diet (LCD). Continuing LCD meal to some strict degree can bring hyperketonemia, which may have beneficial effects on cardiovascular system and anti-cancer in humans.

Keywords: Primate, Ketone bodies (KB), Calorie restriction (CR), Low carbohydrate diet (LCD), Japan LCD Promotion Association (JLCDPA)

INTRODUCTION

Humans have undergone various evolutions for long years. When investigating the physiological functions and pathophysiological impairments in humans, it is important to study other closely related animals. As to the evolution of primates, the brain size has been in discussion until now. The factors for the influence to the evolution are numerous, which are diet quality, social group size, home range area, behavioral and ecological variables. Several comparative datasets of extant primates are investigated for an evolutionary timescale [1]. As a result, there was a significant correlation between brain mass and daily movement, but they were not explained by diet, body mass, social size, or home range. From these, increased mobility may contribute to the increased brain size through primate evolution.

In primate species, neuroendocrine system (NES) has played an important role in controlling the behavior in response to environmental changes [2]. The NES includes some axes which act for regulating growth, stress, metabolism and reproduction. They include the functions of hypothalamus associated with some axes. For the age-related impaired regulation of NES, master circadian pacemaker may be present, that can respond to environment constraints [2].

The changes in the meal pattern may give a large influence to the human. Macroscopic dietary interventions including Calorie Restriction (CR), Low Carbohydrate Diet (LCD), ketogenic diet, a high-fat meal can systemically alter the metabolic situation of the organisms in human and non-human primates [3]. Generally speaking, all kinds of converge on a propensity to strengthen the self-renewal. It may be involved in the importance of metabolism in stem cell homeostasis and disease. Investigation for aging has been conducted by the experiments using short-life model organisms. For the research of aging, non-human primate models have been crucial and indispensable [4]. They provide us the knowledge of domains for aging and examining potential therapeutics against aging intervention.

What is the mechanism and how does diet affect humans? Humans and monkeys are belonged to the same category of the primate. In the field of medical research, it is expected that the results and information obtained by monkeys would be found also in the humans. A variety of research has been progressing in the light of molecular biology, and various studies on diet have been reported so far.

Several research for CR has been reported. In the CR-animals, transcriptional pattern suggests that CR may retard the age-related process by shifting metabolism toward reduced macromolecular damage and elevated protein turnover [5]. By the continuation of dietary CR, life span becomes longer, which would be related with beneficial efficacy on age-related pathology [6]. Previous data showed that negative relationship was observed between increased lifespan and

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decreased calorie intake in mice, which may suggest the role of the regulators of energy metabolism of CR.

Then, for the elongation of life span, metabolic is required from the induction of CR mechanism [7]. According to several studies of mice, flies, worms and yeast, a certain nutrient role may be present. It includes the responsive signaling molecules, which are associated with SIRT 1, PGC-1α and mTOR in CR and aging [8]. Some mechanism may be related to the aging process. The efficacy of CR may be conserved for the aging process in primates.

From mentioned above, it was investigated whether biological effects in monkeys would be found in also human or not. There was a multicenter study in US with sixteen large facilities for diabetes research [9]. It was Look AHEAD Research Group, that reported the significant results. It has the data from more than 5000 obese or overweight T2DM with 13.5 years follow up. The results showed that the reduction of cardiovascular event was not found by intensive lifestyle intervention especially advised for weight reduction [9].

Formerly, incorrect medical information was prevalent concerning the physiological function of ketone bodies (KB). Lots of medical staffs believed that hyperketonemia was risky for human health. However, this was wrong. Nowadays, correct knowledge has been broadly spread, in which KB can become the energy source and product much energy instead of glucose [10]. It is widely believed that glucose can pass and enter freely the blood brain barrier (BBB) in the glucose metabolism, which has small molecular weight as 180. Similarly, main KB consisted of 3-Hydroxybutyric acid (3-OHBA) and Acetoacetic acid (AcAc) can pass BBB freely by usual KB metabolism which has close molecular weights to glucose. If glucose availability may be decreased, KB can change the metabolism and produce in the liver from fatty acids (FA). FA are mobilized from adipose tissue, which show the important role of producing larger source of energy for brain, muscle and heart [11]. KB have been recently argued for the beneficial effects for human bodies. Especially, human shows hyperketonemia in the case of LCD for the treatment of diabetes [12].

For recent years, the comparison between LCD and CR has been discussed. In general, CR means the limitation of fat because of much calorie involvement in fatty food. In the case of LCD, the intake of carbohydrate is decreased. In North American and European countries, Bernstein, Atkins and other researchers have begun and developed LCD [13,14]. On the other hand, authors et al. have initiated LCD and presented clinical efficacy of LCD for various academic papers and opportunities. The research fields include useful ketone bodies, meal tolerance test (MTT), glucose variability, Morbus (M) value, insulinogenic index (IGI) for 70g of carbohydrate, hyperketonemia of fetus-placenta-umbilical cord-newborn-mother [15-18].

As regards to LCD in the medical and health care region, we have proposed three kinds of practical methods through books, seminars and workshops. They are super-LCD, standard-LCD and petite-LCD, in which carbohydrate is included 12%, 26%, and 40%, respectively [19]. Furthermore, our research team has established Japan LCD Promotion Association (JLCDPA) and developed LCD from social point of view.

In summary, humans have evolved from primates. In addition to the mechanism of glucose metabolism, humans and other primates have metabolic pathways producing more energy from KB. Nowadays, KB are becoming widely known for their beneficial effects on the cardiovascular system and anti-cancer in humans [20,21]. Consequently, further development of metabolic research in biology is expected in the future.

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