

## BRIEF COMMUNICATION

# Was there a need for high carbohydrate content in Neanderthal diets?

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## Abstract

**Objectives:** In a recent paper, Hardy et al. (2022, *Journal of Human Evolution* 162: 103105) claim that the physiological Neanderthal requirement for plant carbohydrates may have reached 50%–60% of caloric intake, inferred from modern dietary guidelines and a putative need for high carbohydrate intake in pregnant/breastfeeding women and athletes. The aim of this article is to critically re-examine these arguments under the premise that hominins could adapt to hypercarnivorous diets and low carbohydrate consumption.

**Materials and Methods:** Literature on ketogenic and carnivore diets was retrieved. A case report of a male rugby player voluntarily undertaking a carnivore diet under medical supervision is presented.

**Results:** Human metabolism is highly flexible towards adapting to long-term low carbohydrate intakes by producing and utilizing ketone bodies. The evidence base of dietary guidelines is weak, and carbohydrate intake recommendations for athletes and during pregnancy/lactation are uncertain, making a translation to Neanderthal diets questionable. The studied rugby player maintained his sports performance and health over a 4-months period despite minimal carbohydrate intake.

**Discussion:** Human physiology appears to have an extraordinary ability to utilize ketone bodies as a fuel for the brain and skeletal muscle, in particular also during exercise. The translation of dietary guidelines to Neanderthals and interpretation of studies in subjects not adapted to ketosis may be biased by a “gluco-centric” perspective supposing that high carbohydrate intake is necessary for maintaining health. Allowing for the possibility of keto-adaptation leads to a more coherent integration of archeological and physiological data.

## KEYWORDS

carnivore diet, exercise nutrition, ketosis, paleolithic diet, pleistocene

## 1 | INTRODUCTION

The evolution of hominin diets is not only important to understand our biocultural history, but also from the realization that diet has co-shaped endocrine regulation, metabolism and gene expression of modern humans (Carrera-Bastos et al., 2011; Eaton et al., 1988;

Lemke et al., 2016). Human physiology thus provides important insights for the scientific exploration of Pleistocene hominin diets, complementing other disciplines such as archeology, paleoanthropology, primatology and ethnographic studies of contemporary hunter-gatherers (Hublin & Richards, 2009). Ben-Dor and colleagues recently published several papers in which they integrated a variety of data

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from multiple scientific disciplines supporting the hypothesis that Pleistocene humans, and *H. neanderthalensis* in particular, were hypercarnivores, which eventually derived more than 70% of their nutrition from animal foods (Ben-Dor et al., 2021; Ben-Dor & Barkai, 2020, 2021). Faunal assemblages at Neanderthal sites dominated by large terrestrial mammals (Hoffecker, 2009), nitrogen isotope ratios ( $\delta^{15}\text{N}$ ) from collagen (Bocherens, 2009; Jaouen et al., 2019; Salazar-García et al., 2021) and strontium-calcium and barium-calcium ratios from bone (Balter et al., 2001) have traditionally been interpreted as evidence for the hypothesis that Neanderthals were indeed hypercarnivores. However, the role of plant food consumption is less clear, because the stable isotope data are barely influenced by the consumption of low-nitrogen plants, and plant remains at Neanderthal sites are much less well conserved than bones and collagen from prey. Dental calculus analyses provide evidence of plant consumption by Neanderthals (Hardy et al., 2012; Salazar-García et al., 2021), but it remains unclear whether plants rather complemented a protein- and fat-dominated diet or contributed significant amounts of carbohydrates.

In a recent paper published in the *Journal of Human Evolution*, Hardy et al. (2022) defend the latter hypotheses and emphasize the importance of carbohydrates for Neanderthals, and Pleistocene hominins in general. In their view, “Neanderthals would have needed to include as much as 50%–60% of total energy intake as carbohydrates to provide the energy for their large brains, active lives, hunting activities, and successful reproduction.” To justify this claim, Hardy et al. (2022) mainly refer to physiological arguments, assuming that Neanderthals would have shared a common metabolic physiology with modern humans. Their core arguments can be summarized as follows:

1. Dietary guidelines around the world recommend 50% energy (E%) from carbohydrates for optimal health, a recommendation which is “likely to be largely relevant for hominins, in general” (Hardy et al., 2022).
2. Neanderthals approximately resemble modern rugby players who would require large amounts of dietary carbohydrates to perform well.
3. There is an obligatory glucose requirement of the brain as its main energy source which would translate into a requirement of high dietary carbohydrate intake.
4. Reproduction and infant growth would require high amounts of carbohydrate intake and be compromised on animal-based diets.

Here, I question the validity of the above arguments as a valid support for the hypothesis that carbohydrates played a significant role in the diets of Neanderthals. I am going to argue that the way Hardy et al. (2022) present and interpret the experimental data is biased, because it is deeply rooted within the “glucocentric” context of modern societies that obscures the high metabolic flexibility specific to humans, in particular their exceptionally high capacity of producing and metabolizing ketone bodies. By focusing on human physiology under ketogenic and/or carnivorous diet conditions, including an own

case study, this article complements other multidisciplinary approaches trying to reconstruct the most likely nature of Neanderthal diets. The evidence presented here supports the possibility that Neanderthals in general were able to thrive on a low-carbohydrate or ketogenic diet, without contradicting the consumption of plants in case they were easily accessible.

## 2 | MATERIALS AND METHODS

Relevant literature for some key topics discussed in this paper was retrieved from PubMed, Scopus, and Google Scholar by using appropriate search terms, in particular: “Neanderthals” and “energy expenditure”; “ketogenic diet” and (“pregnancy” or “lactation”); “gluconeogenesis” and “glucose production” and (“low carbohydrate” or “ketogenic”); “dietary guidelines” and “conflicts of interest.” Retrieved papers were evaluated for their relevance to a given topic by screening their title and abstract and additional literature was found by searching through citations in relevant papers.

The presented case study refers to a 26-year old male rugby player who approached us with the wish to be supervised by regular visits to our clinic between October 2019 and February 2020 (4 months), during which he voluntarily underwent a so-called carnivore diet excluding all plant foods. We used a protocol similar to the KETOCOMP study which evaluated body composition and blood parameter changes in cancer patients on a ketogenic diet during radiotherapy (Klement & Sweeney, 2016). The KETOCOMP study protocol had been approved by the ethics committee of the Bavarian Medical Association (Germany). The rugby player consumed one large meal per day between 7 and 8 p.m. or between 10 and 11 p.m. on rest and training days, respectively, which was recorded in a daily food diary. He did not take any nutritional supplements. His activity involved three rugby training and two strength training sessions per week with occasional games on the weekend. His body composition was measured on a bioimpedance scale (seca 515/514 medical Body Composition Analyzer; seca Deutschland, Hamburg, Germany) at baseline and seven times during the carnivore diet. Blood draws were taken at baseline and after 2 and 4 months on the carnivore diet and analyzed in the hospital laboratory as described in detail previously (Klement et al., 2022).

## 3 | RESULTS AND DISCUSSION

Overall, the argumentation of Hardy et al. (2022) appears to be strongly affected by the theoretical presupposition that a significant amount of carbohydrate consumption is necessary for optimizing and maintaining human health. This view is typical for what I refer to as the “glucocentric” paradigm of modern nutrition science and mainstream medicine. In the following, I scrutinize the core arguments listed above from a different perspective, namely the possibility that Neanderthals were well adapted to survive and thrive on a highly carnivorous, low-carbohydrate diet.

### 3.1 | Misguided application of nutritional guidelines

Hardy et al. (2022) repeatedly refer to modern dietary guidelines to emphasize the putatively high requirement for carbohydrates in Neanderthal diets. Dietary guidelines generally recommend limiting animal fat intake and consuming around 50 E% from carbohydrates. The US dietary guidelines are ultimately rooted in the *Dietary Goals for the United States* announced by the senate in 1977, a time when saturated fat was deemed causally related to coronary heart disease and when the public perception changed towards viewing red meat, eggs and dairy as unhealthy (Taubes, 2008; Teicholz, 2014). The advice to reduce cholesterol, total and saturated fat while increasing carbohydrate consumption to 55–60 E% was leaned on guidelines of the American Heart Association which had held tight connections to the vegetable oil and margarine industry; in contrast, the only influence that the meat, dairy and egg producers were able to achieve was that *lean* meats could be advised to eat (Taubes, 2008; Teicholz, 2014). After publication of the Dietary Goals, the USDA was put in charge of implementing them, and the general message hardly changed until today, despite the fact that there was never any high-quality evidence supporting it (Achterberg et al., 2022; Addis & Grootveld, 2021; Harcombe, 2017; Minhas, 2007; Nissen, 2016). In addition, the food industry always had a strong influence on public opinion and dietary guidelines (Herman, 2010) as has been documented, for example, for Coca Cola (Sacks et al., 2017). Of the 20 members of the U.S. 2020 Dietary Guidelines Advisory Committee, 19 had conflicts of interest with the food and/or pharmaceutical industry, many of which are involved in the production of carbohydrate-rich foods (Mialon et al., 2022). Thus, the scientific validity of dietary guidelines must be questioned, because they are not justified by high-quality evidence, but influenced by the food industry, which makes a translation towards dietary needs of Neanderthals highly questionable.

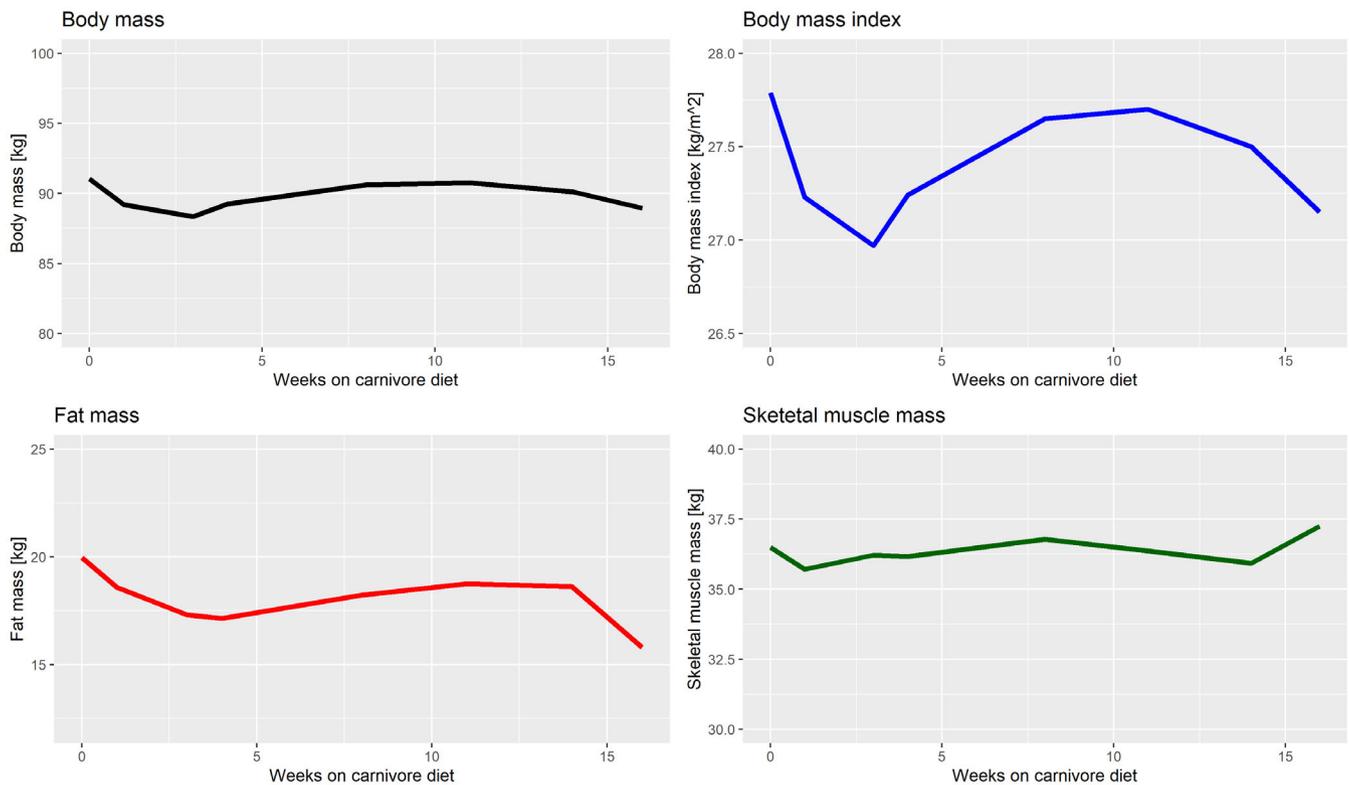
### 3.2 | Carbohydrates and physical activity

By comparing the estimated body mass index (BMI) of Neanderthal individuals with that of athletes from different sports categories, Hardy et al. derive the conclusion that Neanderthals were most similar to Rugby players and hence best adapted to power-based locomotion and ambush hunting rather than endurance running. Then they take the carbohydrate recommendations for elite rugby players (60 E%) as an argument for the putatively high carbohydrate consumption of Neanderthals. If we engage in the analogy between rugby players and Neanderthal individuals, it is important to point out that the nutritional guidelines for the former (aiming to maximize rugby playing performance within the context of abundant and diverse food and nutritional supplement choices) have no epistemic relevance for the diet of the latter who were partly living within environments lacking easy access to edible plants (Guil-Guerrero, 2018; Hoffecker, 2009).

Furthermore, the rugby player studied in our clinic was able to maintain his training and competition performance over a 4-months period on a carnivore diet which provided on average 3150 kcal/day. During this time, his BMI dropped from 27.79 to 27.15 kg/m<sup>2</sup>, while his muscle mass was conserved (Figure 1). During the carnivore diet phase, T3 levels decreased and testosterone levels increased (Table 1), which is expected on a very low carbohydrate diet (O'Hearn, 2018a; Santos, 2017).

While our case study was only a short-term observation (4 months), it nevertheless contradicts the statement by Hardy et al. (2022) that “carbohydrate ... is the only macronutrient that can deliver sufficient energy for high-intensity exercise” (p. 6) or that “[h]igh physical activity requires carbohydrate intake far in excess of that in a ketogenic diet [else] performance is compromised” (p. 16). Statements like these are based on short-term studies showing declines in exercise performance with low carbohydrate intake in subjects not accustomed to eating a low carbohydrate diet (Volek, Noakes, & Phinney, 2015). For example, fig. 2 in Hardy et al. (2022) recapitulates findings from a study of Bergström et al. (1967) in which 3 days of a low carbohydrate diet following quadriceps femoris muscle glycogen depletion in nine healthy subjects led to diminished glycogen regeneration and cycling performance compared to a mixed diet, while a high-carbohydrate diet induced a supercompensation of glycogen stores and significantly prolonged cycling duration. However, several studies allowing for a longer adaption period have shown no negative effects of low-carbohydrate diets on exercise performance in endurance (Phinney et al., 1983; Prins et al., 2019), strength/power (Gregory et al., 2017; Kephart et al., 2018; Paoli et al., 2012; Wilson et al., 2020) and team (Paoli et al., 2021) sports, although some studies found declines in competitive endurance performance (Burke et al., 2017; Zinn et al., 2017). It also appears that training in a glycogen-depleted state can result in favorable training adaptations (Impey et al., 2018). Some athletes choose to consume low carbohydrate or ketogenic diets as a long-term strategy. Volek et al. (2015) have shown that such “keto-adapted” athletes are able to remain stable blood glucose levels during 3 h of treadmill running with minimum carbohydrate intake. Glycogen levels, glycogen depletion and glycogen regeneration were not significantly different from athletes on a high-carbohydrate diet. In addition, keto-adapted athletes achieved their peak fat oxidation at significantly higher intensities ( $70.3 \pm 6.3\%$  vs.  $54.9 \pm 7.8\%$  of  $\text{VO}_2\text{max}$ ) and with significantly higher rates ( $1.54 \pm 0.18$  vs.  $0.67 \pm 0.14$  g/min) compared to athletes on a high carbohydrate diet, a result qualitatively confirmed by Webster et al. (2016).

These data exemplify the extraordinary metabolic flexibility of the human body which—if not consciously being trained—is usually lost in contemporary individuals due to the constant availability of carbohydrate-rich foods (Freese et al., 2018). Therefore, it appears possible that Neanderthals were highly keto-adapted and thus able to live a highly active life without obligatory high carbohydrate consumption. Finally, similar to the dietary guidelines for the general population, the translational relevance of dietary guidelines for peak performance of athletes to possibly keto-adapted Neanderthals appears questionable.



**FIGURE 1** Body mass, fat mass, and skeletal muscle mass development of a 26-year old male rugby player during a carnivore diet maintained over 4 months. Measurements were made in a fasted state and with an empty bladder on a bioimpedance analysis device as described by Klement and Sweeney (2016)

**TABLE 1** Hormone profile before and during a carnivore diet in a male rugby player

Parameter	Baseline	Day 61	Day 118
TSH (mU/L)	2.18	2.58	1.73
T3 (pg/ml)	3.11	2.51	2.20
T4 (ng/dl)	1.25	1.15	1.03
Testosterone (ng/ml)	7.29	7.52	10.6
Parathyroid hormone (pg/ml)	27.3	19.2	19
25(OH)D <sub>3</sub> (ng/ml)	27.5	20.2	16.6

### 3.3 | Biased interpretation of cerebral energy metabolism from a glucocentric perspective

An indication for evolutionary adaptations towards habitual low carbohydrate intake is the human's superior ability to produce and metabolize ketone bodies during fasting or ketogenic diets compared to most other mammals (Gammeltoft, 1949). Even in hibernating animals, ketonemia is much lower than in humans who fast or are in nutritional ketosis—in black bears and ground squirrels, average ketone body concentrations of  $0.73 \pm 0.31$  and  $1.62 \pm 0.13$  mmol/L, respectively have been measured (Krulowicz, 1985; Shimozuru et al., 2016). Primates appear to have a similar ability to reach ketosis than humans, although data supporting this statement are only based on urinary and not serum ketone body measurements (Friedemann, 1934, 1942;

Naumenko et al., 2020). Neanderthals would have profited from an adaptation towards an efficient fat- and ketone-based metabolism not only during times of total starvation or general calorie restriction conditions, but also if they concentrated on obtaining animal foods. The latter point is emphasized by some authors who question that humans had to endure frequent starvation,<sup>1</sup> for example, Amber O'Hearn:

The comparison between ketogenic diets and starvation can make sense only from a worldview in which high carbohydrate diets are the default. Humans are naturally in ketosis without caloric deficit or inadequate protein levels so long as carbohydrates are restricted. This ability appears to be unique to our species, and is likely intimately related to our large brains, as it tracks developmentally with brain growth [...] This unique ketogenic facility in the fed state strongly suggests a selective advantage to ketosis that co-opted the previous function of starvation fuel. For this advantage to have been selected and developed to this degree, it must have been in frequent operation. That is, the low carbohydrate condition must have been prevalent. (O'Hearn, 2018a)

Thus, new insights could be gained if we start to look beyond the glucocentric paradigm of modern societies according to which

cerebral glucose oxidation is the *conditio sine qua non*. It is important to point out that during a ketogenic diet, one third of the brain's energy requirements may be met by ketone bodies which are utilized at a rate inversely proportional to that of glucose (Courchesne-Loyer et al., 2017). During long-term starvation, ketone bodies even become the dominant energy source for the brain (Cahill, 2006) and can completely cover its basal energy requirements (Achanta & Rae, 2017). In general, the uptake and oxidation of ketone bodies in the brain is almost linearly proportional to their plasma concentrations (Mikkelsen et al., 2015; Pan et al., 2000), contradicting the claim of Hardy et al. (2022, p. 5) that “Glucose cannot be replaced as an energy source, but ... [only] be supplemented.” Because ketone bodies also provide more ATP per mol oxygen than glucose, they have been labeled a “superfuel” (Cahill & Veech, 2003). Besides this, the ketone body  $\beta$ -hydroxybutyrate is now recognized for several beneficial effects in the brain such as induction of brain-derived neurotrophic factor (Sleiman et al., 2016), protection against reactive oxygen species and reduction of neuroinflammation (Achanta & Rae, 2017).

If cerebral energy requirements in Neanderthals, cited as 127 g glucose for a male by Hardy et al., were partially met by ketone bodies, gluconeogenesis alone could have covered the remaining glucose requirements. Bisschop et al. (2000) have measured postabsorptive gluconeogenesis in six healthy men after 11 days of a ketogenic diet with 15 E% from protein as  $6.3 \pm 0.2 \mu\text{mol kg}^{-1} \text{min}^{-1}$  (123 g/day for a 75 kg male). Veldhorst et al. (2009) measured a gluconeogenic rate of  $171 \pm 10 \text{ g glucose/day}$  in 10 healthy men who consumed a short-term 30 E% protein ( $\approx 190 \text{ g/day}$ ), zero-carb diet. Finally, Brosnan (1999) calculated that gluconeogenesis from a physiological mixture of amino acids alone could yield 135 g glucose/day, and that much higher rates are possible with lactate or glycerol as substrates. Thus, if Neanderthals were hypercarnivores they would likely still have been able to meet their large brain's metabolic demands through ketogenesis and gluconeogenesis. Alternatively, a daily intake of about 150 g carbohydrates would have been sufficient to fully account for cerebral glucose consumption. Using estimates for the total energy expenditure of Neanderthal males which—depending on body mass, climate and physical activity—might have ranged between  $\approx 3300$  and  $6700 \text{ kcal/day}$  (Churchill, 2006; Froehle & Churchill, 2009; Snodgrass & Leonard, 2009; Sorensen & Leonard, 2001; Venner, 2018), 150 g carbohydrates would constitute between 9 and 18 E%, which is far below the 50–60 E% recommended by dietary guidelines and suggested by Hardy et al.

### 3.4 | Reproduction and infant growth do not require 50%–60% carbohydrate diets

The major argument made by Hardy et al. in favor of high carbohydrate consumption by Neanderthals is the carbohydrate demand of pregnant and breastfeeding mothers. Specifically, they point out the importance of placental glucose uptake for fetal growth and survival (e.g., Baumann et al., 2002) and the additional glucose demand of breastfeeding mothers for producing lactose which would result in

overall minimal glucose requirements of 140 g glucose/day. One can estimate the daily energy requirement (DER) of pregnant or lactating women by the formula

$$\text{DER} = (\text{BMR} + [\text{PR}] \text{ or } [\text{LC}]) \times \text{PAL}, \quad (1)$$

where BMR is the basal metabolic rate, [PR] or [LC] stand for the additional energy costs of pregnancy or lactation, respectively, and PAL is the physical activity level (Hockett, 2012). Using an estimate for a Neanderthal woman's BMR of 1465 kcal/day (Snodgrass et al., 2009) and  $[\text{LC}] = 1.9 \text{ MJ/day}$  ( $\approx 450 \text{ kcal/day}$ ) (Butte & King, 2005), this results in an estimated energy requirement of 3830–5745 kcal/day for PAL values between 2 and 3. Thus, the minimal glucose requirement of 140 g glucose/day for a lactating woman cited by Hardy et al. (2022) would account for only 10–15 E%. Analogously, Hockett (2012) used Equation (1) to estimate the DER of pregnant Neanderthal women as  $\approx 3800$ – $5500 \text{ kcal/day}$  by assuming  $[\text{PR}] = 400 \text{ kcal/day}$ . Hockett also showed that an isocaloric diet derived exclusively from large terrestrial herbivores would have resulted in toxic levels of protein intake as well as insufficient intake of folate and vitamin C. Analogously, Guil-Guerrero (2017) concluded that a diet dominated by large terrestrial mammals could not have contained sufficient quantities of vitamin C and omega-3 fatty acids. These modeling studies imply that the Neanderthal diet would have necessarily included a greater diversity of food types of which some may have contained larger amounts of monosaccharides or starch (Hardy, 2010; Power et al., 2018), but many others only small to negligible amounts of carbohydrate (e.g., eggs, birds, fish, tortoises, mushrooms, green leafy vegetables, and nuts) (Blasco et al., 2022; Weyrich et al., 2017).

However, the amount of carbohydrates needed to grow and nourish healthy babies is much less clear than suggested by Hardy et al. (2022). For example, Lavie et al. (2019) retrospectively compared 37 women who adhered to a Paleolithic diet during pregnancy to 39 women on a standard diet and found that the former had significantly better glucose tolerance, iron and hemoglobin levels and less days off work during pregnancy than the latter. There was no significant difference in pregnancy complications or adverse neonatal outcomes between both groups. Although socioeconomic status and physical activity levels were not controlled for, this study shows that a diet typically providing only 10–30 E% from carbohydrates (Cordain, 2002; Klement et al., 2021) does not negatively affect pregnancy and even may exert beneficial effects compared to a modern standard diet. There are even some case studies from pregnant mothers on long-term ketogenic diets due to epilepsy (van der Louw et al., 2017) or GLUT-1 deficiency syndrome (Kramer & Smith, 2021) that provide a proof-of-principle that healthy pregnancies and normal child development are possible with very low carbohydrate consumption. Although this cannot be generalized to the general population as a whole, we should acknowledge the possibility for homeostatic functioning of the human body during a diet that is considered extreme only from the glucocentric perspective. Tanner and colleagues have pointed out “that there is insufficient evidence to support current recommendations on necessary carbohydrate intake and avoidance of

ketones" (Tanner et al., 2021, p. 287). Indeed, the human placenta both takes up and synthesizes ketone bodies (Hosoya et al., 1960); these are not only energetic fuels for the fetal brain, but potentially are necessary for encephalization (Tanner et al., 2021).

There are also case reports of unproblematic adherence to a ketogenic diet during lactation such as Tan-Smith et al. who described the case of a healthy mother successfully implementing a ketogenic diet with a gradual decrease of carbohydrate intake to 70 g/day which resulted in a 134% increase of her milk's energy density and managed the epileptic seizures of her infant. However, there are also case reports of lactation ketoacidosis which appears to be a very rare yet dangerous side effect of ketogenic diets in breastfeeding mothers. A literature review of 12 cases by Nnodum et al. (2019) suggests that the development of lactation ketoacidosis in non-diabetic, non-alcohol drinking mothers on a ketogenic diet appears to be associated with extremely low carbohydrate intake (<50 g/day) combined with additional stressors such as insufficient energy intake (e.g., starvation), feeding twins (also see Alsomali, 2021) or infection (also see Liu & Bertsch, 2021). Some of these women had been adherent to a strict ketogenic diet for many years without complications including pregnancy and the initial post-partum period (e.g., Osborne & Oliver, 2022), so that it could be argued that lactation ketoacidosis might have been a threat to Neanderthal women even if they were well adapted to a ketogenic diet. Nevertheless, as estimated above, a diet containing 10–15 E% from carbohydrates would very likely have been sufficient to prevent lactation ketoacidosis during this special life period, so that a general claim for the necessity of 50–60 E% in Neanderthal diets is not supported by the data.

Compared to the evidence for a necessity of high plant food consumption during pregnancy and lactation, evidence for the importance of animal foods is much stronger. This is because the necessary micronutrients for brain growth and functional development from early stages *in utero* up to adulthood are much more abundant and bioavailable in animal than in plant foods (Broadhurst et al., 2002; Saladino, 2020). The conversion of the polyunsaturated fatty acid  $\alpha$ -linolenic acid (18:3 $\omega$ 3), the major precursor of long-chain polyunsaturated fatty acids occurring in plant foods, into the essential docosahexaenoic acid (DHA) (22:6 $\omega$ 3) has low efficiency of  $\leq 1\%$ , and most of  $\alpha$ -linolenic acid (>60%) is oxidized, even under DHA deficiency conditions (Plourde & Cunnane, 2007). This implies that DHA likely was obtained directly from animal foods (Plourde & Cunnane, 2007; Thomas Brenna, 2002).

Evidence also exists that carbohydrate-rich diets with high plant food consumption exacerbate dietary nutrient requirements. As our case study illustrates, T3 levels decrease on very low carbohydrate diets (O'Hearn, 2018a), and as a consequence may require lower intakes of iodine (Kopp, 2004), which Dobson (1998) described as a rare nutrient for Neanderthals. Besides sea food (if it was available), a major source of iodine for Neanderthals could have been the thyroid gland of land vertebrates, while goitrogens in plant foods may have further increased the need for dietary iodine intake (Lindeberg, 2009). Another example is ascorbic acid (vitamin C) which competes with glucose for intracellular uptake, so that its requirement is significantly

increased on high carbohydrate intakes (Clemens & Tóth, 2016; Ely, 2006). Indeed, vitamin C deficiency (scurvy) was unknown in traditional populations consuming minimal amounts of carbohydrates such as the Inuit and Indigenous North Americans, indicating that animal sources of vitamin C are sufficient within the context of a low carbohydrate diet (Price, 2010). Finally, many edible plants accessible by Neanderthals contain anti-nutrients such as tannins, phytates and oxalates which bind to and directly decrease the bioavailability of micronutrients (Cordain, 1999; Gibson et al., 2018; Lindeberg, 2009; Norton, 2018). A diet low in these anti-nutrients may have increased bioavailability of animal-food-derived nutrients and resulted in good conditions for reproduction, cognitive development and physical activity despite a lack of high carbohydrate intake.

To summarize: the physiological requirement of carbohydrates for successful reproduction is not well known, so that inferences for the Neanderthal diet derived from modern carbohydrate recommendations for pregnant and lactating women are highly uncertain. Much more certain is the requirement for brain-specific nutrients which are highly abundant and bioavailable in animal foods but whose bioavailability may be reduced with high plant intakes. Together, these points imply that the current knowledge about the physiology of reproduction does not support a Neanderthal diet containing 50–60 E% carbohydrates.

#### 4 | CONCLUDING REMARKS

It is always worthwhile to critically question long-established narratives. The motivation of Hardy et al. (2022) to critically question the narrative of Neanderthals as the prototype of a mainly carnivorous human species should therefore also be welcome. However, their inference that Neanderthals had to consume 50–60 E% from carbohydrates appears at odds with the archeological evidence for high meat consumption, as they also acknowledge. To solve this apparent paradox, Hardy et al. proposed three possibilities:

1. Neanderthals were genetically adapted to a high-meat diet, just as contemporary arctic populations are adapted to a high-fat diet by a genetic variant of *CPT1A* which results in reduced hepatic fat oxidation and ketogenesis (O'Hearn, 2018b). However, this possibility is considered unlikely due to the spatiotemporal consistency of the archeological data.
2. Neanderthals survived on a suboptimal low-carbohydrate diet, but could not thrive. This possibility is dismissed due to the longevity, cultural and technological achievements of Neanderthals.
3. The stable isotope evidence classifying Neanderthals as top-level carnivores is wrong or outweighed by the physiological evidence for high carbohydrate requirements, especially for successful reproduction. This is the favored option of Hardy et al.

As I have argued, the physiological evidence for high carbohydrate requirements presented by Hardy et al. is weak and lacks translational relevance if one considers the possibility that

Neanderthals were well-adapted to ketosis. I have presented evidence in favor of this possibility which comes from the growing literature on the physiology and application of ketogenic and/or carnivore diets.

To gain further insights into the possibility for keto-adaption in Neanderthals I would encourage future experimental research in human subjects consuming very low carbohydrate diets excluding all food groups that would not have been available to Paleolithic humans. Diets such as the “Paleolithic Ketogenic Diet” (Clemens et al., 2018; Clemens & Tóth, 2019), “Carnivore Diet” (Lennerz et al., 2021) or “Zero-carb diet” (Protogerou et al., 2021) have recently gained popularity among certain social groups, which provides a unique opportunity to study human metabolism and the possibility to “thrive” on such diets. I agree with Chang and Nowell (2016) who proposed to use the popularity of Paleolithic diets to start a dialogue between the public and evolutionary scientists, and I propose to especially include Paleolithic-type diets with high meat content or completely excluding plants. Our case report and the classic study of the arctic explorer Dr. Vilhjalmur Stefansson and K. Andersen who underwent a 1-year meat-only diet under medical supervision (McClellan et al., 1930) provide evidence for the medium-term safety of carnivore diets in humans. Two other recent studies showed that there is a large population of individuals who voluntarily follow a long-term hypercarnivorous diet because it makes them feel well and healthy (Lennerz et al., 2021; Protogerou et al., 2021). Finally, traditional populations such as the Inuit have been known for their low consumption of plants and may have thrived in a state of chronic ketosis despite their *CPT1A* variant (O’Hearn, 2018b). If it is indeed possible to thrive on a hypercarnivorous diet in our times (O’Hearn, 2020), the putative anomaly posed by Hardy et al. between basic physiological carbohydrate requirements and the extensive archeological evidence would vanish.

#### AUTHOR CONTRIBUTIONS

**Rainer J. Klement:** Conceptualization (equal); data curation (equal); formal analysis (equal); methodology (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

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#### CONFLICT OF INTEREST

Rainer J. Klement reports no conflicts of interest related to this research.

#### DATA AVAILABILITY STATEMENT

All data used in this article are available from the author upon reasonable request.

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#### ENDNOTE

<sup>1</sup> A cross-cultural comparison study by Berbesque et al. indeed shows that warm-climate hunter-gatherers experience significantly less famine than other subsistence societies including agriculturalists (Berbesque et al., 2014). This may be due to the great flexibility of the hunter-gatherer lifestyle and may well apply to early Homo living in habitats with abundant animal food resources.

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