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To Restore Health, "Do we Have to Go Back to the Future?" The Impact of a 4-Day Paleolithic Lifestyle Change on Human Metabolism – a Pilot Study.

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Abstract
On their way from the Stone Age via the Agricultural Revolution to current high-tech conditions, humans lost their primal foraging behavior. Today, energy expenditure is not necessary anymore for gathering nor hunting, and metabolic diseases are epidemically arising wherever our original Paleolithic lifestyle is turning into a modern sedentary lifestyle. In this pilot study, we followed through the concept that a radical change towards a Paleolithic hunter-gatherer lifestyle could serve as therapy against any metaflammatory disease, even in the short term. Thirteen healthy adult volunteers were transferred to the DELUX National Park (Germany and Luxembourg) for four days and three nights, where Stone Age conditions where mimicked. Thirty-eight biochemical and bioelectrical parameters were measured from participants before and after this relocation. Body weight (-3,9%), body fat (-7,5%), body mass index (-3,8%), visceral fat area (-14,4%) and metaflammation-related parameters (fasting glucose = -18,2%; fasting insulin = -50,1%; HOMA = -57,8%) decreased significantly. C-reactive protein, as the main indicator for low-grade inflammation, increased up to an average of 169,6 %. Our data show that returning to our Paleolithic roots may have positive effects on risk factors commonly associated with metabolic disorders, such as obesity and type 2 diabetes. These findings may lead the way to further research to answer the question whether the already existing metabolic conditions and/or autoimmune and neuroinflammatory diseases could be influenced by a Paleolithic lifestyle.

Keywords
Paleo diet, Metabolic syndrome, Low-grade-inflammation, Metainflammation, HOMA-index, Sedantary lifestyle

Cover Page Footnote
The authors are indebted to Dr. Annette Quade, Head of the ambulatory health care center Dr. Quade & Kollegen in Cologne, for funding the laboratory samples and Changhun Jo, CEO of InBody Germany, who provided us with an InBody720® System.

Introduction

Along the way from stone age via agriculture revolution to modern high tech conditions, humans lost their primal foraging behavior. In western society, energy dense food is always available and human existance does not rely on exercise to survive anymore. More than 2,5 million years of mankind, abundant physical activity and fasting during the day as well as food intake after sunset (which serves as a reward for successful hunting and gathering) represented the general case. Therefore, humans developed an extraordinary flexible metabolic system, trained by daily and seasonal fluctuations of food and water supply, thermic and immunological challenges as well as hiking and hunting under fasting conditions.

At the present day, the ongoing ingestive behaviour stands in contrast to our circadian rhythm, which enables the cortisol awakening response after sunrise. Cortisol works as a catabolic stress hormone to mobilize stored glucose and fatty acids supplying energy for the locomotor system. In western societies, the evolutionary evolved self-provision of energy is no longer used by the muscular system due to our predominantly sedantary lifestyle. As a result of new habits such as permanent food availability, increased meal frequency, high glycemic load foods and a significant regression of muscle energy expenditure, humans in all western countries establish a constant energy surplus with persistent alternating peaks in blood sugar and elevated basal insulin levels [1] [2]. Gradually, this toxic mix concurrently overrules the physiologic tolarance of our metabolic system, ending up in visceral obesity, glucose intolerance, hyperinsulinemia and low-grade inflammation (LGI) – the pathway to western diseases [3] [4] [5].

This phenomenon can currently be observed in hunter-gatherer, or primal living societies such as those in the area of the Pacific States, whose traditional way of living is turning into an urban, sedantary lifestyle in record time [6] [7] [8]. In contrast, the incidence of type 2 diabetes (T2D) in established modern societies has been increasing for decades. According to the 2003 edition of the diabetes atlas [9], the number of type 2 diabetics for 2025 was predicted with 330 million people worldwide. Today, already 387 million diabetics populate planet earth [10]. An increasing number of middle-aged sedentary people suffer from pancreatic insufficieny although this organ was designed to function for a potential life expectancy of approximately 80 years. Before the discovery of insulin in 1921 by Banting and Best, every insulin insufficient patient died within days. As opposed to insulin as the only blood sugar lowering hormone, diverse hormones such as adrenalin, cortisol, thyroid hormones and growth hormone are vital for increasing blood sugar. Since the beginning of human beings, the endocrine ability to raise the blood sugar level, rather than lowering it, has been of an overriding importance for survival reason. First, the origins of agriculture emerged around 10.000 BC in the middle-east and are considered to be the greatest evolutionary

transformation in the history of our species, characterized by the cultivation of grains and domestication of livestock. Second, the industrial era of the past 200 years with hallmark inventions such as sanitization, automobiles, refrigerators, televisions, telephones etc. and last but not least the ongoing digital revolution, shifting important life fundamentals (e.g. communication and economic subsitance) into the world wide web, have turned the tables towards a maladaptation within humans conditioned by inactivity and high glycemic energy are captured. Since the late 19th century western killer diseases based on metaflammation are steadily increasing [11] [2].

Metaflammation – the connection between obesity, type 2 diabetes and low-grade inflammation

Obesity, the consequence of a constant imbalance between energy intake and energy expenditure, is widely accepted as LGI [12]. In response to a progressive accumulation of unfavorable fatty acids along with elevated counts of macrophages in visceral adipose tissue, a transition towards a greater proinflammatory subtype occurs [13] [14]. These adipocyte-specific M1-like cells exude pro-inflammatory cytokines such as interleukin-1-beta (IL-1b) and tumour-necrosis factor alpha (TNF-alpha) [15]. As a result of this, a state of chronic LGI spreads throughout the entire body. It is well established that hyperglycaemia, based on high glycemic food intake, supports the pro-inflammatory activity of macrophages [3] [4]. Driving force of this visceral inflammation is TNF-alpha, a multifunctional immunologic semiochemical. TNF-alpha is essential for local and systemic inflammation. In cooperation with IL-1-beta, this cytokine duo amplifies insulin resistance (IR) [16], because IR does not appear, if TNF-alpha is blocked by anti-TNF-alpha-drugs [17].

A prediabetic state, described as metabolic inflammation (metaflammation), does not comply with classical defence mechanisms of the immune system against pathogens like viruses, bacteria or fungi [4] [18]. Esposity [19] demonstrated that experimental induced hyperglycemia leads to a significant increase of the pro-inflammatory cytokines TNF-alpha und IL-6. Raised glucose levels in blood vessels lead to a vascoconstrictive, prothrombotic inflammation, measurable via C-reactive protein (CRP), a liver-derived acute-phase protein, which stimulates acute infectious and non-infectious inflammation via IL-6 [20] [21]. In contrast, pancreatic insulin, immediately secreted due to raising blood glucose levels supresses inflammation [22] [23] [24]. Human studies show that low-dose insulin infusions block intracellular inflammatory mediators such as nuclear-factor-kappa-B (NF-kB) [25] [26]. In a state of chronic insulin resistance, this anti-inflammatory effect is reduced – the hotbed for a systemic low-grade inflammation, known for its severe impact on western killer diseases i.e. cardiac infarction, cancer and neurodegeneration.

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Exercise under fasting conditions – the key factor for prevention and therapy of metaflammation?

Over more than 2,5 million years ago, exercise represented a vital foreaging behaviour with existential impact, whereas food intake was depending on seasonal disposability, physical power, coincidence, intuition and knowledge of environment [27] [28]. Subjects, who move before they eat show a substantially lower postprandial inflammatory reaction. Each intake of nutrients causes a postprandial immune response [29] [18], based on the production of non-inflammatory molecules such as lactoferrin, immunglobuline A (IgA) and lysozyme in order to prevent an energy-consuming stimulation of innate immune cells [30]. This non-inflammatory reaction becomes pro-inflammatory if lactoferrin, IgA and lysozyme are absent or reduced, as commonly occuring in overweight individuals [31]. A postprandial inflammatory reaction can be observed, if meals contain high amounts of fat along with with refined sugar or linoleic acid [32] [33]. This also applies when humans consume grain-fed animal meat [34] [35] [36]. As a consequence, the postprandial inflammation acts as the catalyst for the development of endothelial dysfunction, cardiovascular disease, obesity, IR and chronic LGI [37] [30] [38] [39].

Animal experiments show that caloric restriction (CR) and intermitted fasting (IF) can suppress the development of a huge number of illnesses and extend life expectancy. In mouse models, CR increases the lifespan by 30-40%. CR further shows significant anti-inflammatory effects by reducing high sensitive CRP and TNF-alpha [40] [41] [42]. Accordingly, CR due to skipping meals or IF combined with adequate units of exercise (including oxidative and glycolytic parts) could be very important for the prevention of metainflammation and its associated diseases.

In our pilot study, we followed the broad idea that a radical change from sedentary lifestyle to a metaphorical paleolithic hunter-gatherer condition of living could reverse modern lifestyle related derailments such as hyperglycaemia, hyperinsulinemia, hypercholesterinemia and LGI serving as an empirical model for a multi-purpose and all natural therapy against metabolic and inflammatory diseases. We would like to emphasize our initial interest in the synergistic effects of a multifactorial lifestyle change, where participants exercise before they eat and drink (foreaging behavior), ingest their main meal at night (as a reward due to successful hunting and gathering) and eat only organic, non-processed foods according to the paleo diet regime [43] [44] [45], while living within the scope of their biorhythm determined by the rise and setting of the sun, without any time pressure and the use of digital devices or access to the internet.

Methods and Materials

Measurements

In total, 38 biochemical and bioelectrical measurements were collected from participants directly before their departure as well as after their return from the excursion. Blood samples were drawn by a medical doctor, stored in a cooling bag and immediately transported to a laboratory in Cologne. The bioelectrical measurements were also carried out on-site before and after the excursion by using the Body Composition Analyzer InBody720®. The duration of activity and physiological output was measured with SenseWear® armbands and the portable navigation system Etrex Vista HCX.

Participants

All participants of our study were students, scientists, physicians and other health professionals who were interested to participate as volunteers. They accepted Jens Freese as the coordinator for this study, signed an informed consent and were educated about the course of action during the intervention. A group of 13 healthy adult volunteers was relocated for a period of 4 days and 3 nights in the DELUX National Park.

***Table 1**: Demographic and anthropometric features of participants at the enrolment: The mean age of subjects (6 female and 7 male) was 39 (+/- 8.1) years, with a range of 22 to 49 years. The BMI of subjects ranged from 19.3 kg/m^2 to 27.4 kg/m^2 with 9 subjects classified as normal weight and 4 classified as overweight. One subject was a smoker. Of the 13 subjects, 7 were classified as exercise trained. Subjects were rated as exercise trained if they regularly performed a combined minimum of three hours per week of anaerobic and aerobic exercise of moderate to high intensity. Collectively, subjects were relatively healthy, active men and women who did not rely on any prescription drugs. Eligibility and classification was determined by completion of a pre-admission questionnaire.*

	Participants
Race	Caucasian
N	13
Female	6
Age (years)	39 (± 8.1)
Normal weight BMI < 25 (kg/m^2)	9
Overweight BMI > 25 (kg/m^2)	4
Exercised trained (> 3 hrs/week)	7
Smoker	1
Prescription drugs	0

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Study Design

Participants lived and slept outdoors with no,shelter in the national park DELUX, bordering the countries Germany and Luxembourg. They were accompanied by a guide without profound local knowledge using map and compass. He was the only group member equipped with a cell phone for logistic, organizational and emergency reasons. Every morning, the group filled up water cans in a nearby holiday apartment at the very edge of the National Park, which was especially rented for this intervention. Each participant received a daily ration of of fruits, nuts and tubers with the instruction not to eat before noon, for the purpose of hiking at least 4 hours under fasting conditions. This instruction should ensure an intermittend fasting period of at least 12 hours a day, consisting of 8 hours sleep and not less then 4 hours of physical activity before food intake. In the apartment, coordinators stored all instruments for the measurements. Every night, carefully prepared paleo meals were delivered to the group by car since wild hunting aquires month-long training for a special licence in Europe. Coordinators have determined a meeting point with the guides and handed over food plates to group members. Rubbish was completely removed by the cordinators. The dietary composition of foods was aimed to reconstruct a paleolithic diet based on the recommendations of Cordain and others [44] [43]. For calculation of caloric intake and nutrient dispersion we used the National Nutrient Database for Standard Reference [46].

Statistical Analysis:

The data meets the requirement of being normally distributed and of an interval level of measurements. Arithmetic average and standard deviation were calculated. Statistical comparisons of mesurements before (pre) and after (post) excursion were made using student t-tests for dependent samples. Presence or absence of statistical significance was determined using a two tailed hypothesis test. The level of significance was chosen with following borders of significance and their markings: $p \geq 0.05$ insignificant, $p < 0.05$ significant (*), $p \leq 0.01$ very significant (**), $p \leq 0.001$ highly significant (***) [47].

Results

The daily macronutrient ratio of carbohydrates (22%) and protein (24%) in our study corresponded with the boundaries of the paleo diet, the ratio of fat (54%) was 7% higher than recommended. This elevated fat intake is not considered to interfere with the concept of the paleo diet since food choices have been met accordingly. A detailed breakdown of our results is shown in Table 2. The majority of measured biometric values changed significantly when baseline was compared with the 4-day outcome.

Regarding changes in body composition, the total body fat (%) decreased marginal, whereas all other data measured by the body composition analyzer InBody720® such as weight, muscle mass, BMI, visceral fat area, fat free mass and body fat in kg were reduced very and high significantly. The biochemical data listed in table 4 shows highly significant changes in fasting glucose, insulin and HOMA-index, representing the main values to indicate IR. Lymphocytes and thrombocytes show a weak significant change, while CRP increased excessively in some if not all subjects. Neither HDL-cholesterol, LDL-cholesterol nor Adiponectin were mentionable affected by the intervention.

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Table 2: *The choice of foods as listed was consumed over 3 days. All foods were measured by weight (grams). To estimate total caloric intake and macronutrient ratios, the USDA Nutrient Interactive Database [46] was used. Daily energy intake for each participant came to an average of 1567 calories. Differences may result from fibre and organic acids in foods. The ratios of macronutrient intake during the intervention were calculated with 22% carbohydrates, 54 % fat and 24 % protein.*

	Weight (g)	Kcal	Protein (g)	Fat (g)	Carbohydrate (g)
Almonds	6700	9843	359.55	848.81	366.35
Apple	3600	1872	9.36	6.12	497.16
Apricots	1300	624	18.2	5.07	144.56
Blackberries	500	215	6.95	2.45	48.05
Blueberries	1300	741	9.62	4.29	188.37
Butter	400	2868	3.4	324.44	0.24
Carrots	3300	1353	30.69	7.92	316.14
Cauliflower	1300	299	23.92	5.85	53.43
Grapes	1600	1104	11.52	2.56	289.6
Green Beans	2600	910	49.14	7.28	204.88
Grilled Chicken	3900	9321	1064.7	530.4	0
Kiwi	1300	793	14.82	6.76	190.58
Olive-Oil	200	1768	0	200	0
Onions	1000	440	13.6	1.9	101.5
Peach	1800	702	16.38	4.5	171.72
Pear	3500	1995	12.6	4.9	533.05
Radish	1300	208	8.84	1.3	44.2
Red Currant Berries	700	392	9.8	1.4	96.6
Roast Beef Tenderloin	3600	11664	860.4	885.6	0
Salad	700	91	9.45	1.54	15.61
Salmon Filet	3300	6072	902.88	247.5	0
Tomatoes	745	134	6.56	1.49	28.98
Turnip	600	132	4.26	0.48	30.36
Walnuts	1200	7416	288.72	708	118.92
Zucchini	700	161	7.28	2.73	26.53
Total Calories		61118	3742.64	3813.29	3466.83
Daily Calories per Person		**1567**			
Macronutrient Ratios			**24%**	**54%**	**22%**

Table 3: Both, physiological output and sleeping behaviour were measured with SenseWear® armbands. To quantify the daily hiking distance and, the portable navigation system Etrex Vista HCX from Garmin was used. Daily averages were calculated for hiking distance (15 km), elevation gain (845 m) and hiking duration (3.42 h). Other activities associated with nomadic hunting and gathering were: swimming, climbing, lifting and building a fire. Total average activity came to 5.92 hours, inactivity 10.18 hours and of that the average sleeping time added up to 7.9 hours.

Activity	Duration (h)	Distance (km)	Elevation Gain (m)
Hiking	3.42	15	845
Other	2.5		
Sleeping	7.9		
Inactivity	10.18		

Table 4: Changes in biochemical data over the course of the intervention. Values represent the mean ± SD. P-values shown are uncorrected.

(n=13)	Pre	Post	Change	p
Leukocytes (nL)	5.87 (± 1.877)	6.149 (± 1.793)	4.8%	0.178
Erythrocytes (pL)	4.689 (± 0.507)	4.812 (± 0.535)	2.6%	0.124
Hemoglobin (g/dL)	14.015 (± 1.487)	14.4 (± 1.75)	2.7%	0.184
Hematocrit (%)	41.877 (± 3.973)	42.946 (± 4.37)	2.6%	0.157
MCV (fL)	89.469 (± 2.974)	89.377 (± 3.246)	-0.1%	0.736
MCH (pg)	29.915 (± 1.31)	29.91 (± 1.307)	0.0%	0.947
MCHC (g/dL)	33.438 (± 0.904)	33.462 (± 0.896)	0.1%	0.886
RDW (%)	12.877 (± 0.442)	12.5 (± 0.476)	-2.9%	0.000***
Thrombocytes (nL)	212.46 (± 63.413)	235.54 (± 51.247)	10.9%	0.046*
Neutrophils (%)	59.092 (± 7.005)	62.262 (± 5.248)	5.4%	0.151
Lymphocytes (%)	31.054 (± 6.63)	26.7 (± 3.685)	-14.0%	0.030*
Monocytes (%)	7.469 (± 1.282)	8.132 (± 2.704)	8.9%	0.351
Eosinophils (%)	1.769 (± 1.017)	1.646 (± 1.224)	-7.0%	0.629
Basophils (%)	0.615 (± 0.254)	0.592 (± 0.26)	-3.7%	0.673
Fasting Glucose (mg/dL)	87.154 (± 4.669)	71.308 (± 9.903)	-18.2%	0.000***
Gamma GT (U/L)	16 (± 5.73)	15.308 (± 5.023)	-4.3%	0.168
Total Cholesterol (mg/dL)	182.77 (± 34.274)	182.31 (± 34.683)	-0.3%	0.88
HDL (mg/dL)	77.015 (± 15.321)	78.362 (± 16.075)	1.7%	0.654
Triglycerides (mg/dL)	53.769 (± 16.692)	44.231 (± 9.671)	-17.7%	0.072
LDL (mg/dL)	99.154 (± 27.136)	98.169 (± 29.86)	-1.0%	0.73
LDL / HDL Quotient	1.331 (± 0.446)	1.299 (± 0.507)	-2.4%	0.793
CRP high sensitive (mg/L)	0.395 (± 0.654)	1.065 (± 1.495)	169.6%	0.034*
Insulin (uU/mL)	4.223 (± 1.099)	2.108 (± 0.682)	-50.1%	0.000***
Homa - Index	0.912 (± 0.268)	0.385 (± 0.174)	-57.8%	0.000***
Adiponectin (ug/mL)	7.668 (± 3.256)	7.122 (± 2.754)	-7.1%	0.115

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Table 5. *Changes in body composition over the course of the intervention. Values represent the mean ± SD. P-values shown are uncorrected.*

(n=13)	Pre	Post	Change	p
Weight (kg)	69.7 (± 13.389)	66.992 (± 12.78)	-3.9%	0.000***
Body Fat (kg)	11.554 (± 5.506)	10.685 (± 5.37)	-7.5%	0.002**
Muscle Mass (kg)	32.681 (± 7.226)	31.909 (± 6.967)	-2.0%	0.001***
BMI (kg/m²)	22.559 (± 3.249)	21.698 (± 2.944)	-3.8%	0.000***
ICW (L)	26.6 (± 5.535)	26 (± 5.328)	-2.3%	0.001***
ECW (L)	16.108 (± 3.292)	15.285 (± 2.887)	-5.1%	0.000***
Proteins (kg)	11.485 (± 2.396)	11.231 (± 2.318)	-2.2%	0.002**
Minerals (kg)	3.937 (± 0.8)	3.8 (± 0.755)	-3.5%	0.000***
Visceral Fat Area (cm²)	48.769 (± 29.147)	41.731 (± 26.862)	-14.4%	0.000***
Fat Free Mass (kg)	58.146 (± 11.986)	56.308 (± 11.251)	-3.2%	0.000***
Total Body Water (L)	42.708 (± 8.802)	41.285 (± 8.201)	-3.3%	0.000***
Lean Body Mass (kg)	54.908 (± 11.338)	53.185 (± 10.641)	-3.1%	0.000***
Body Fat (%)	16.6 (± 7.178)	16 (± 7.513)	-3.6%	0.062

Figure 1: *Fasting Glucose reduced from 87.153 to 71.308 mg/dL during the course of the intervention. This change was highly significant (p<0.000).*

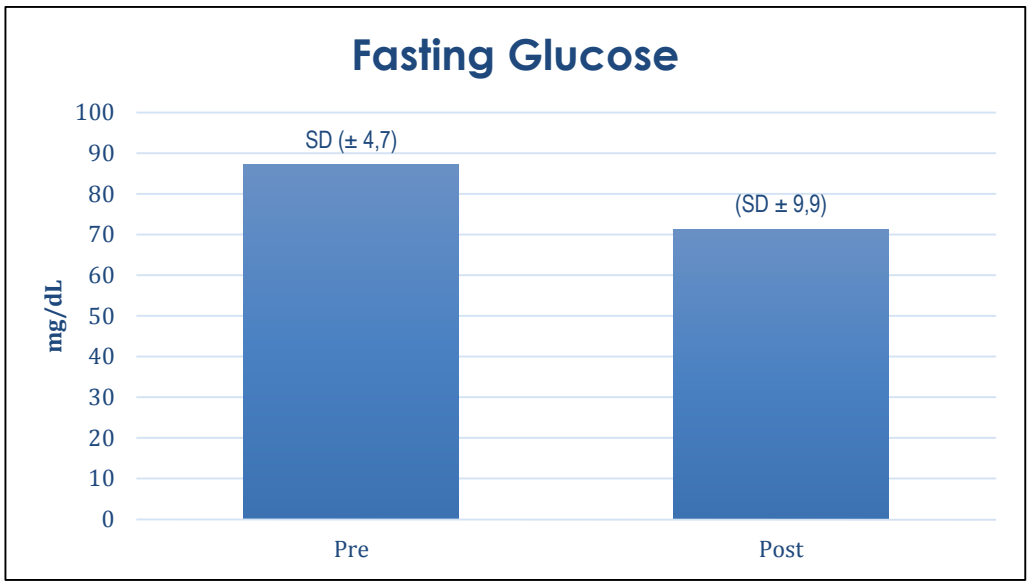


Figure 2: *Insulin reduced from 4.223 to 2.108 uU/mL during the course of the intervention. This change was highly significant (p<0.000).*

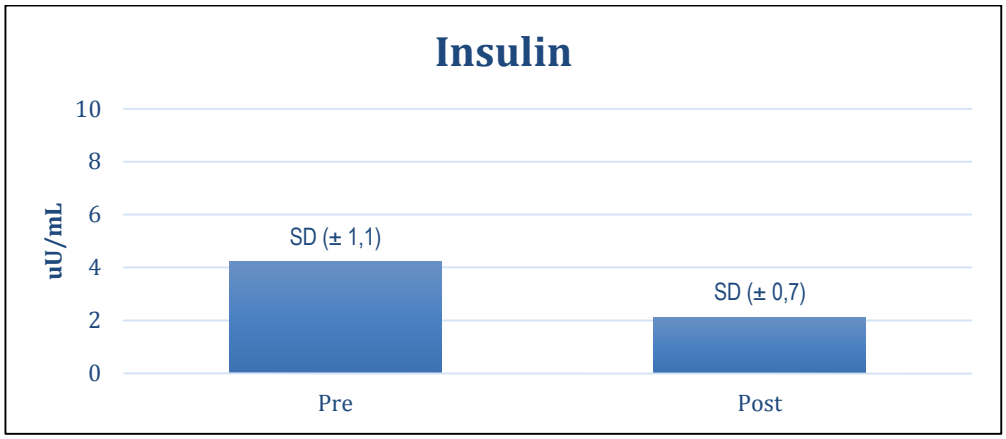


Figure 3: *Homa Index reduced from 0.912 to 0.385 during the course of the intervention. This change was highly significant (p<0.000).*

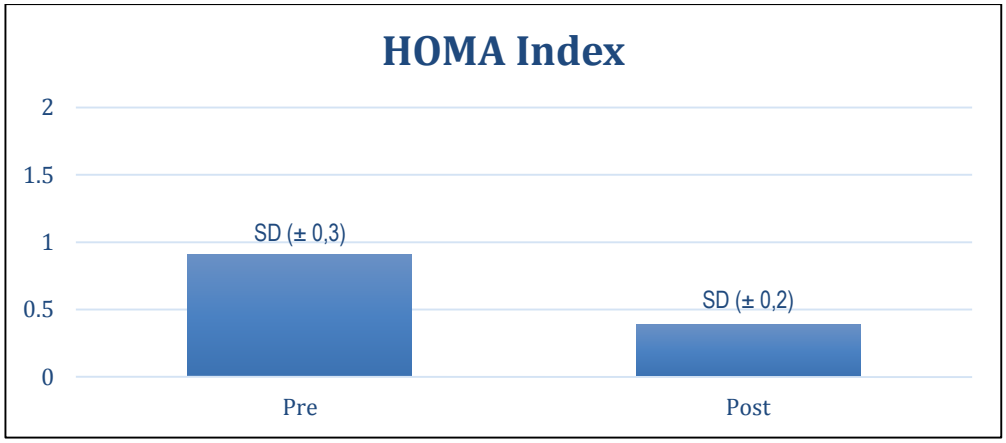


Figure 4: *High sensitive CRP-levels increased from 0.395 to 1.065 mg/L during the course of the intervention. This change was significant (p<0.034).*

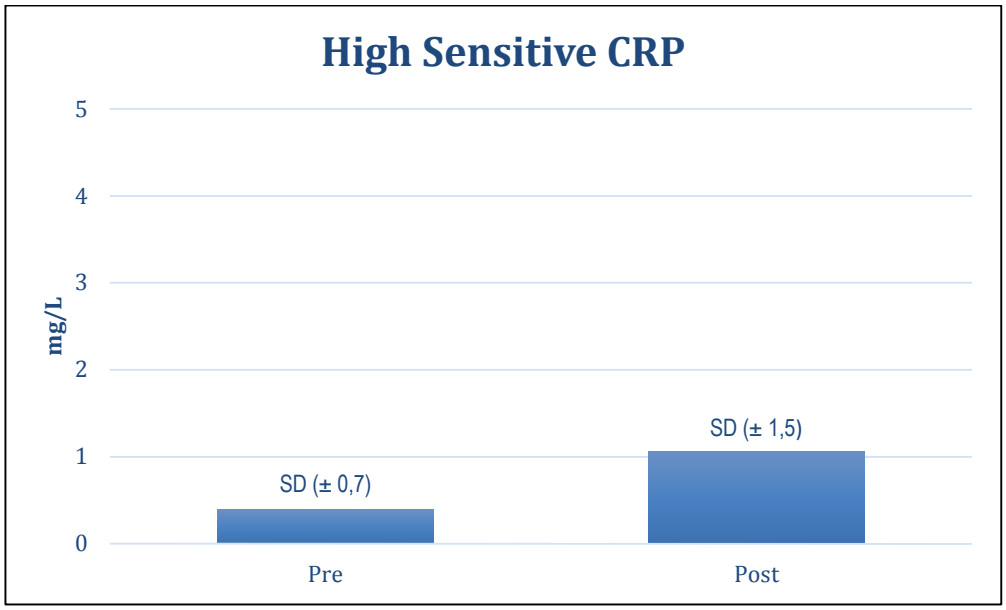


Figure 5*: Body weight reduced from 69.7 to 66.99 kg during the course of the intervention. This change was highly significant (p<0.000).*

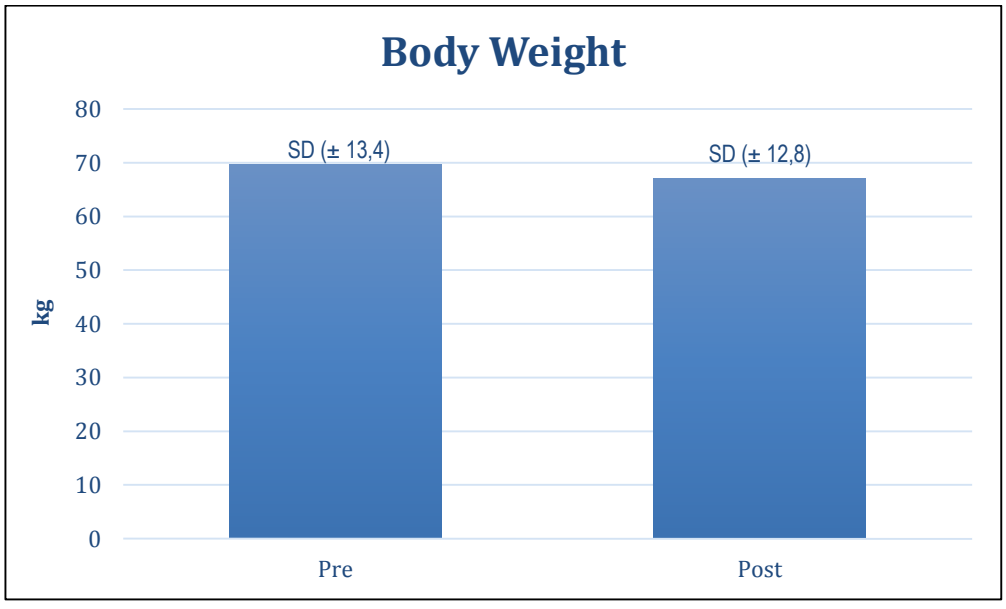


Figure 6: *Body fat (kg) dropped from 11.554 to 10.685 kg during the course of the intervention. This change was very significant (p<0.002).*

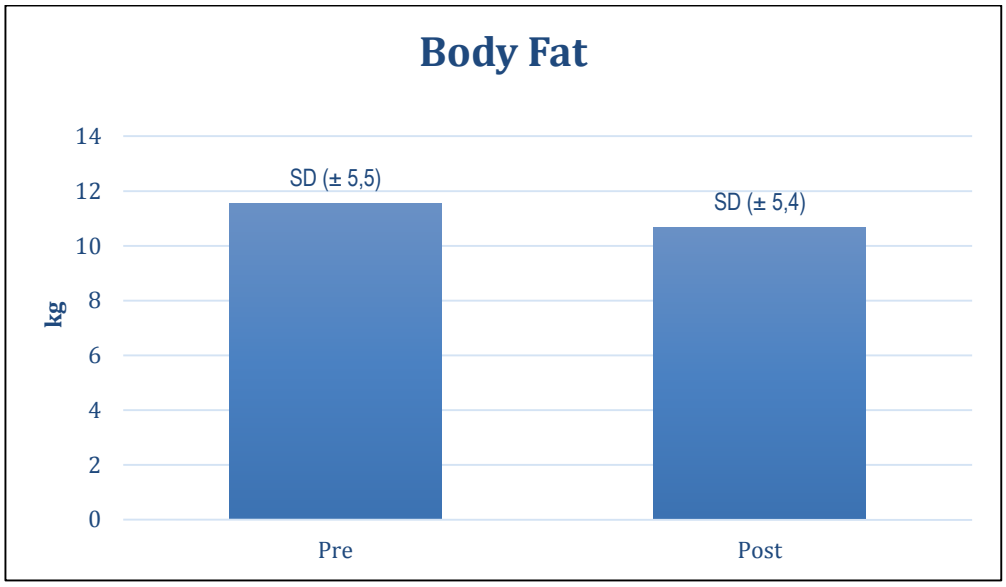
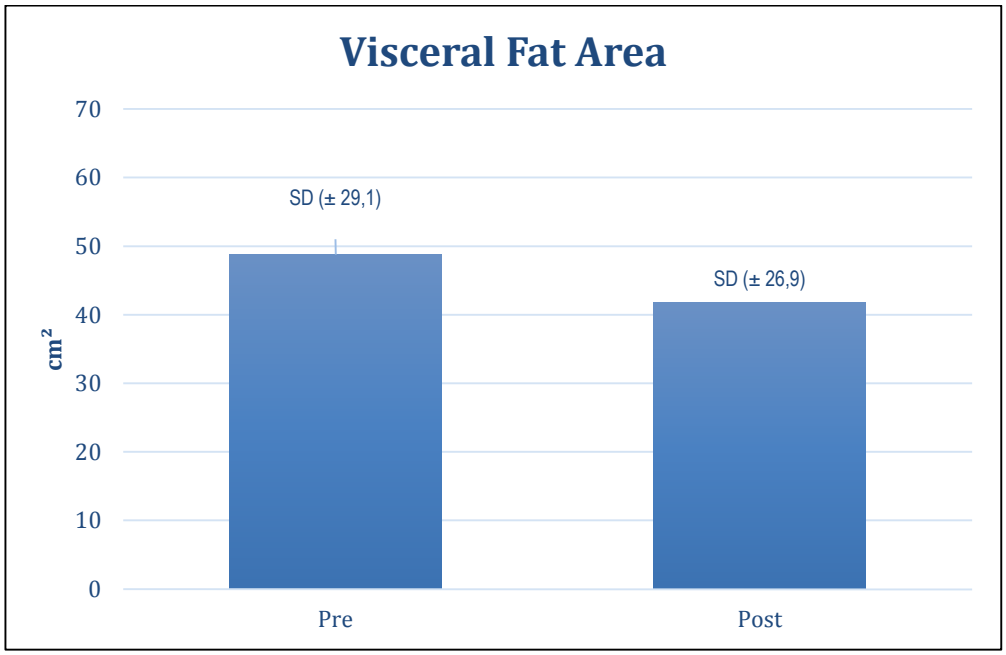


Figure 7: *The visceral fat area dropped from 48.769 to 41.731 cm² during the course of the intervention. This change was highly significant (p<0.000).*



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Discussion

The pattern of food distribution (>12 h fasting) combined with a reduced caloric intake nearly reached the dietary regime of intermittent fasting (IF) (24 h fasting) in our study. IF without malnutrition has been shown to have numerous benefits on metabolic risk factors for chronic diseases in several mammalian species [48] [49] [41]. Nowadays, modern humans have to deal with an oversupply of food and caloric energy. Excessive merchandising of foods rich in refined grains, sugars and oils intensifies the old instinct to search for energy dense foods in view of our on energy deprivation adapted brain. Unfortunately, the search usually comes to an end with the quick access of the nearby refridgerator or visit at the corner store. In other words, since human survivorship has been shaped by industrialized diets and sedentary ways of life, no energy expenditure is necessary anymore for gathering or hunting food. Paleontological records show that early humans had to adapt to the ambient ressources in different geological environments, suggesting flexibility in food intake was part of human evolution [50]. This is still reflected by the diversity of diets among extant hunter and gatherer populations. Their diets vary around the world in their ratio of plant and animal foods as well as in macronutrient proportions [51]. In modern times, we lost this evolutionary programed flexibility in food intake and food selection. Unsurprisingly, the constant availability of dietary energy intake – being able to eat anything at any time, is far away from our nature and closely related to the prevalence of chronic diseases.

The rapid metabolic effects in our study display that a short but multifactorial lifestyle change in the scope of a simulated paleolythic environment led to an accelerated recovery of energy homeostasis in a short period of 4 days. Anthropometric determinants such as body weight (-3,9%), body fat (-7,5%), body mass index (-3,8%) and visceral fat area (-14,4%) decreased significantly. These improvements were expected due to the relatively low caloric intake (1567 ckal per day) combined with a high quantum of physical activity (15 km hiking per day), partially under fasting conditions, contrasting the ever present inactivity in todays sedentary lifestyle.

More unexpected we noted extravagant changes of parameters related to metaflammation. Outstandingly, fasting glucose (-18,2%), insulin (-50,1%) and HOMA (-57,8%) dropped highly significant. In contrast, CRP as the main indicator for LGI, raised to an average of 169.6 %. We suppose, that living in the wild stimulates the innate immune system as shown by Qing [52] and Park [53] via activation of proinflammatory pathways in order to anticipate evolutionary old danger signals such as bacteria, viruses, insects or predators.

This data shows that going back to our paleolithic roots can have positive effects on risk factors that are commonly associated with metabolic disorders such as obesity and type 2 diabetes. Our findings suggest further research in

relation to the question as to whether existing metabolic conditions or autoimmune and neuroinflammatory diseases can be influenced or perhaps cured by a paleolithic lifestyle change. The individual factors responsible for the observed benefits of our 4-day immersion into the evolutionary underpinnings of diet and lifestyle are difficult if not impossible to allocate because of the multiple radical changes compared to industrialized. Beside CR and IF, inevitable spontaneous physical activity before food and water intake might be one of the main beneficial factors of our intervention. Another aspect is the complete dissconnection from common sources of stress associated with our modern lifestyle such as time-pressure, traffic-noise and visual complexity in exchange with old danger signals (thirst, hunger, very high or cold temperatures)surrounded by forested landscape. Considered as natural stressors, thirst, hunger and other danger signals have accompanied us for most of our evolutionary history. Finally, a factor analysis was not the intention of this pilot study. Further investigations could aim for precise distinctions between the multiple parameters presented in our study, in order to recover our ancient metabolic system during the rapid shifts in human diet. It might be possible that ultimately, the synergistic effects concurring in this intervention are the main drivers responsible for such promising results.

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