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"Impact of the timing of food intake on metabolic parameters and health"

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Andra Pitic, BSc

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1. INTRODUCTION

Cardiovascular diseases, cognitive disorders and diabetes are among the most important public health burdens worldwide, as they are responsible for the death and disability of millions every year. [95] Obesity and dislipidemia significantly increase the risk of cardiovascular diseases and diabetes [96] and eating behaviours are known to be main influencing factors for chronic diseases. [97] For the prevention and therapy of these risk factors and diseases, there is a lot of research, which focuses on the quantity and quality of the diet. Yet, the temporal aspect of food intake is starting to gain attention as a main influencing factor on metabolic parameters and health. [98]

Intermittent fasting (IF) refers to an eating behaviour, where food intake is either restricted to a certain time frame (time restricted feeding, TRF) or it refers to fasting every other day (alternate day fasting, ADF) or fasting for two consecutive days in a week. [1, 2, 3, 6]

Animal studies show significant positive impacts of IF on the life-span [7, 8], body weight and body composition [9]. Even with no overall caloric restriction, studies show mice under an ADF regime present lower glucose and insulin concentrations and higher β-hydroxybutyrate levels [3]. Studies show that even a reversal of insulin resistance is possible in obese mice, along with lower levels of leptin and greater adiponectin values. [12, 13, 14] Time-restricted feeding (TRF) protects mice from hepatic steatosis and inflammation and enhances their motoric coordination. [15] Regarding cardiovascular diseases, studies show that mice undergoing an ADF regime showed protection against myocardial infarction. [16, 18] Furthermore, ADF has a positive impact on cognition as mice had better responses against neuronal degeneration. [21, 25, 26, 36]

Human studies also show positive impacts of IF regarding body weight and body composition [45, 46, 47]. Metabolically, IF also presents benefits in humans by reducing low density lipoprotein (LDL), triglycerides (TG) [48], insulin- like growth factor 1 (IGF-1) [54] and C-reactive protein. [58]

In some cases, the benefits of IF could be attributed to caloric restriction. Time-restricted feeding is a type of IF, which presents benefits regardless of caloric reduction. [58, 59] Weight loss, lower insulin levels and lower blood pressure were consequences of TRF when the participants were subjected to food intake especially in the morning and midday, which indicates the positive association between TRF and the circadian rhythm [50, 59, 60-64]

The aim of this master thesis is to review the current evidence on the health benefits of IF, to explain the heterogeneity of some of the data appearing in these studies and to assess whether IF as a lifestyle has a positive impact on a large variety of subjects, aged between 18 and 65 years old, healthy or suffering from chronic diseases and whether food intake outside of the circadian rhythm has a negative impact on health parameters of these subjects.

2. LITERATURE OVERVIEW

2.1. Types of intermittent fasting

There are various types of intermittent fasting (IF) but we can differentiate periodic fasting (PF) from time-restricted feeding (TRF). Periodic fasting refers to less frequent but longer fasting periods which can go from two up to twenty-one days or more. The fasting period includes fasting or "fasting-mimicking-diets" (FMDs). Time-restricted feeding is a type of IF and it refers to restricting food intake to a period of 8 hours a day or less on all days. [1] There are also other types of IF, for example diets which involve alternate day fasting (ADF) [2, 3], restricting energy intake every other day [4, 5] or on two consecutive days in a week. [6]

2.2 Impact of intermittent fasting on metabolic parameters and health of animals and humans

2.2.1. Impact of intermittent fasting on animals

The impact of IF on animals may differ quantitatively according to the type of IF and the species involved, but there seem to be some reoccurring metabolic impacts that characterize a fasting period, such as low blood glucose levels, decrease or depletion of glycogen stores, fatty acid mobilization and ketone body synthesis, lower circulating leptin levels and higher adiponectin values. [4, 14] IF also seems to elevate alertness and cognitive abilities. [99]

Alternate day fasting (ADF) and time-restricted feeding (TRF) are the two principal types of fasting used in rodent studies. [1] One of the first cues that IF may have a positive impact on animal health was a study from 1982 showing that rats which were put on a ADF at a young age got to almost twice the age of the rats on an ad libitum diet, with an increase of 83% in life span. [7] Then a study in 1983 showed that if rats were exposed to ADF in middle age, they showed an increase of 30-40% in lifespan compared to the ad libitum fed control group. [8]

2.2.1.1. Impact on body weight and body composition

There is plenty of evidence in the literature regarding the positive impact of IF on body weight in animals. One recent study aimed to analyse and quantify the impact of IF on body weight and body composition of animals consuming different diets fed male C57/BL6 mice a diet consisting of 45 % fat (HFD) for 8 weeks and then divided them into four groups. One group received the HFD ad libitum, another was on an ADF-HFD, the third group was fed ad libitum with a diet consisting of 10% fat (LFD) and the last one received an ADF-LFD. The results after 4 weeks showed a decrease in body weight of 13% for the ADF-HFD group and a decrease of 18% for the ADF-LFD compared to the ad libitum fed HFD. A significant increase of 12%-13% was observed in lean mass for the ADF-LFD group when compared to the HFD and ADF-HFD group. All interventions resulted in a lower body fat ranging from 40%-52% [9].

2.2.1.2. Impact on metabolism

The study on the male C57/BL6 mice, which analysed the impact of different types of diets with or without IF also looked on changes occurring in metabolic parameters. As a result an improved insulin tolerance area under the curve for all interventions (ADF-HFD, ADF-LFD and LFD) was observed with a decrease ranging from 22% to 42%. [9].

In order to determine whether these changes are a result of the IF or of mere caloric restriction, another study also working with male C57BL/6 mice managed to eliminate this variable by feeding the mice the same amount of food whether they were on ADF or fed ad libitum. They did this by feeding the ADF mice on their feeding days twice as much as the ad libitum fed mice, which led to similar body weights for both groups at the end of the study. Nevertheless, there were significant differences in glucose and insulin concentrations at the end of the intervention. These were significantly lower in the ADF mice, showing that even without caloric restrictions IF has beneficial effects on the metabolism of mice. Also, it was interesting to notice that insulin levels decreased in the ADF group even more compared to a third, caloric restricted group which received only 40% of the amount of the ad libitum fed group (LDF, limited daily feeding), which suggests a differentiation in the ways IGF-1 and insulin concentrations are being regulated. When looking at ketone levels, which can serve as an energy source [10] and which appear to induce neuroprotective effects [11], fasting serum concentrations of β-hydroxybutyrate were two times greater in the ADF group compared to the ad libitum fed control but were decreased in the LFD group when compared to the control [3].

Another study aiming to investigate whether IF alone can protect against diet-induced obesity used a different type of fasting called TRF and set male C57BL/6J mice on a high caloric diet with 60% of energy coming from fat and another group of mice on a diet with 13 % fat, either fed time-restricted (8:16 fasting) or ad libitum. Even though all groups received the same amount of calories the high-fat time-restricted fed mice were protected against body weight gain in comparison to the ad libitum high-fat fed group. Also, the high-fat time-restricted fed group was protected against hyperinsulinaemia, hepatic steatosis and inflammation and showed better motor coordination. [15]

There is evidence in the literature even of a reversal of insulin resistance noticed in obese mice following an ADF regime. Decreased levels of leptin and insulin [12] and an increase in adiponectin were other consequences of IF on mice. [12, 13, 14]

2.2.1.3 Impact on cardiovascular diseases

To assess whether IF has any positive effects on cardiovascular diseases and its consequences, this study compared the repercussions of a myocardial infarction (MI) on rats that underwent ADF for 3 months prior to the event and on rats that were fed ad libitum. The results showed that there were differences in the size of the MI, the ADF group having a 2 times smaller MI 24 hours after the

induction of coronary artery litigation. Also, a difference in the number of apoptotic myocytes between the two groups was observed, as it was 4 times smaller in the ADF group. Another difference was noticed in the inflammatory response, which was significantly less in the ADF rats. Having continued the ADF regime versus the control group further differences were noticed 10 weeks after the MI with the ADF group showing no left ventricular remodelling and expansion of the MI compared to the ad libitum fed rats which did show both. [16]

Another study quantified infarct size in mice with and without IF. Adult C57BL/6 mice, which underwent an ADF regime for 6 weeks prior to the incident showed a significantly reduced infarct size in both females and males when compared to the ad libitum fed mice. When looking at Lamp 2 heterozygous mutant mice (a membrane protein 2 connected with lysosome) they noticed that the defence was no longer existent, which indicates that a functioning autophagy-lysosome mechanism is crucial for myocardical homeostasis when undergoing a ADF regime and that it also plays a role in ischemic shielding. [17]

Aiming to assess the mechanism through which IF offers protection after a myorcardial ischemia (MI) in rats, it was concluded that it happens through the cell survival PI12kinase/Akt activation and the VEGF pathway. Two weeks after provoking an MI in rats by occluding the left coronary artery they put half of them on an ADF regime and observed them for the following 6 weeks. The ADF group showed a significantly better survival rate than the ad libitum fed ones with a survival rate of 88.5% for ADF and 23% for the ad libitum fed ones. The cardiac functions were also significantly better preserved in the ADF group compared to the ad libitum fed ones. Looking at the molecular mechanism, it seems that angiogenic factors like Hypoxia-inducible factor 1-alpha (HIF-1- α), Brain-derived neurotrophic factor (BNDF) and Vascular Endothelial Growth Factor (VEGF) were significantly up-regulated in the fasting groups compared to the controls. Furthermore, anti-apoptotic factors like Protein kinase B (Akt) and B-cell lymphoma 2 (Bcl-2) were also up-regulated in the ADF rats compared to control. [18]

When looking to observe the effects of IF on male rats regarding oxidative stress and fibrosis in the heart, they were put on an ADF regime at 2 months of age. The ad libitum fed group showed that there was a significant increase in oxidative stress and fibrosis in the heart of the 24 months old rats and higher inflammatory cytokine levels compared to the younger rats which were 6 months old from the same group. The IF group on the other hand was protected against all these ageing effects, with the elder IF group showing levels for all these markers similar to the ones found in younger rats. [19]

With increasing age, there appear to be some hypertrophy markers in the heart of rats alongside the better known rise in plasma BNP associated with heart failure. These changes are likely to be connected to the increasing activation of the signaling pathways ERK1/2 and PI3Kγ, which in turn

appear to be down-regulated by an ADF regime alongside the repairing of the STAT3 activity, thus decreasing the pathological age-related hypertrophy inducement in rats. [20]

2.2.1.4 Impact on neurological disorders

There is also evidence showing that ADF has positive impacts on aging in animals, protecting the cognitive and sensory-motor function in rodents. [21]

Alzheimer's disease is a neurodegenerative disorder marked by a gradual deterioration of the cognitive function, which is related to the amyloid β-peptide (Aβ) plaques and neurofibrillary tangles. [22]

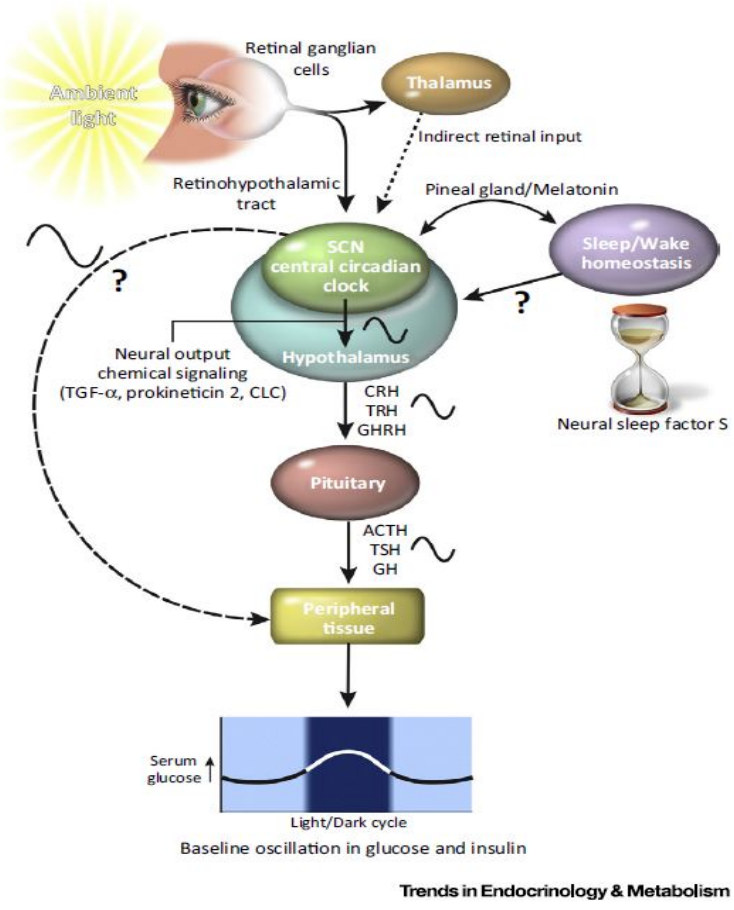
Before the use of transgenic animals, like we do nowadays, models for neurodegenerative diseases were created using neurotoxins. For the models of Alzheimer's disease toxins like kainic acid and domoic acid were used in order to produce hippocampal injuries. [23] It was observed that by keeping rats on an ADF diet for a few months before the use of kainic acid their neurons showed a better response against degeneration. [24] In order to mimic the accumulation of Aβ related to age and typical for Alzheimer's disease, models of transgenic mice have been created, which show familial mutations in the β-amyloid precursor protein (APP) and possibly also a presenilin 1 mutation. [25]

Triple transgenic 3xTgAD mice, which show mutations in APP, presenilin 1 and Tau were used in a study which aimed to compare the impact of CR and IF on age-related behavioural deficits using the Morris swim task and open field apparatus. At the age of three months the female and male mice were divided into 4 groups including non-transgenic ad libitum fed, transgenic ad libitum fed, transgenic 40% caloric restriction and transgenic intermittent fasting with feeding every other day. At the age of 10 months half of the mice underwent the behavioural tests, which resulted in a decreased exploratory activity on behalf of the transgenic mice fed ad libitum when compared to the non-transgenic and to the transgenic mice on CR or IF. At 17 months of age the transgenic mice on CR and IF showed greater exploratory activity and a better performance in the swimming test when compared to the transgenic mice fed al libitum. Also, the results presented lower Aβ and phospho-tau in transgenic CR mice compared to the control group, but these markers were not decreased in the transgenic IF mice. This suggests that IF may offer protection against the negative impact of Aß and tau pathology and that CR and IF can protect against a deterioration of cognitive function regardless of Aß and tau pathologies. [22] The mechanism by which this protection occurs has not yet been identified but it may be related to some consequences of IF like the decrease in oxidative stress through the expression of antioxidant enzymes, keeping the mitochondrial function upright [1] and higher levels of autophagy [17] and of neurotrophic factors like cortical and striatal BDNF and basic fibroblast growth factor (bFGF). [26]

The neurodegenerative mechanism which occurs in a stroke implies metabolic and oxidative stress, damage or death of the nerve cells through excitotoxicity, apoptosis and inflammation. [27, 28] There

are a few proteins and signalling pathways that can offer protection during a stroke. These are BNDF and bFGF, protein chaperons like the heat schock protein 70 (HSP70) and glucose regulated protein 78 (GRP78). Also antioxidant enzymes play a protective role, like superoxide dismutases and heme oxygenase-1 (HO-1) [29, 30, 31, 32, 33] Studies show that an ADF diet a few months prior to an ischemic injury can protect against brain damage in animal models. Even though the exact mechanism through which IF offers this protection has not been identified, it is suggested that it involves the increase in BDNF and bFGF, antioxidant enzymes like heme oxygenase1 and protein chaperones HSP70 and GRP78. Other ways through which IF may protect against brain damage are decreasing levels of pro-inflammatory cytokines like tumor necrosis factor α (TNFα), Interleukin 1 beta (IL1-ß) and Interleukin 6 (IL6). [26] Also, reducing oxidative stress induced by lipopolysaccharide [34, 35] and decreasing leptin levels while increasing ketone levels may also be ways of neuroprotection that IF provides. [36]

2.2.1.5 The mechanism of circadian biology and the impact of time restricted feeding (TRF) in animals



To understand the correlation between the impacts of early time restricted feeding on animals and humans, we must first take a look at the mechanism of the circadian clock. The circadian clock is a system which influences both physiological and behavioural rhythms in animals and humans like sleep, body temperature, metabolic parameters and hormone production, which are linked to cues from the environment like light-dark cycles and timing of food intake. [39]

Fig. 1 Circadian control of the endocrine system. The suprachiasmatic nucleus (SCN) where the central circadian clock is located receives information of light noticed through the retinohypothalamic tract from retinal ganglian cells. This information is also registered here indirectly from the thalamus. Sleep/wake cycles are another system which oscillates

and is mainly led by the volume of neural sleep factor S. There is one factor which can synchronize the central circadian system and the sleep/wake homeostasis, namely melatonin. The hypothalamus releases hormones like corticotropin-releasing hormone (CRH), thyrotropin- releasing hormone (TRH) and growth hormone releasing hormone (GHRH) when it receives neural and chemical cues from the SCN. These hormones lead the pituitary gland to produce adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH) and growth hormone (GH) in a circadian rhythm. This impacts peripheral tissues, which act in different manners according to the time of the day. In this figure we see the oscillation of blood glucose during a light/dark cycle, which rises in the late evening and arrives at its peak in the middle of the night and reaches its lowest point in the morning. CLC = cardiotrophin-like cytokine; TGF-α = transforming growth factor. [87]

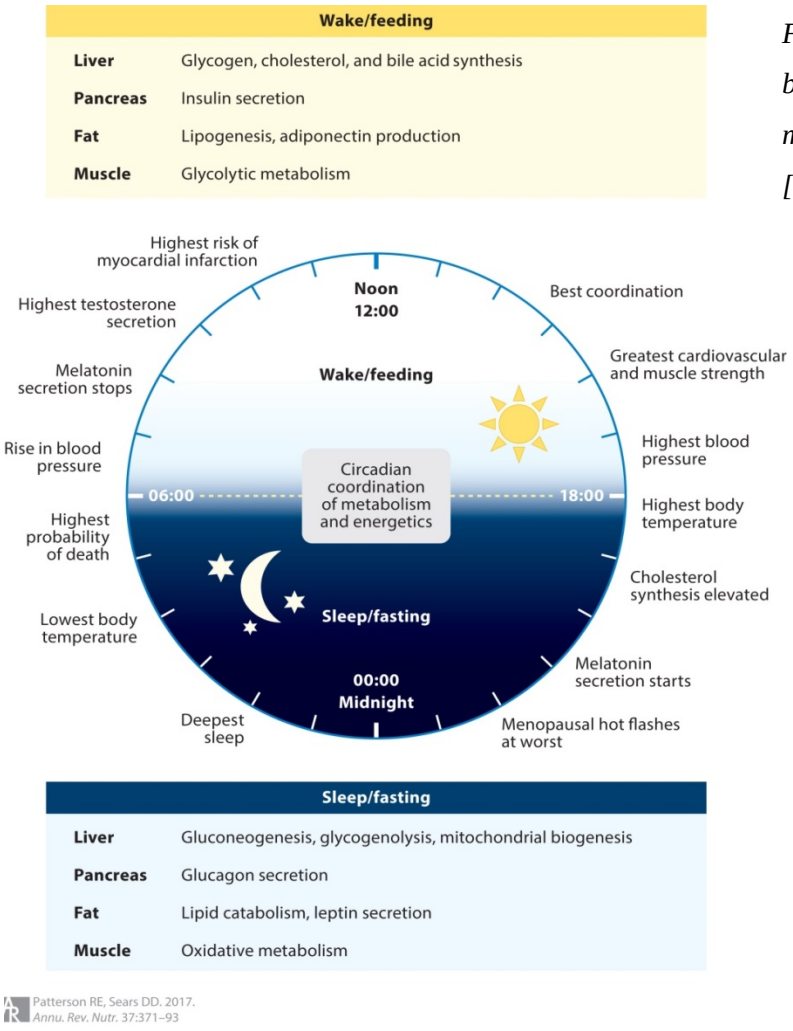


Fig. 2 "Circadian regulation of behaviors, hormones, physiology, metabolism, and energetics." [40]

The master circadian clock lies in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus and is controlled by clock genes like CLOCK, BMAL1, PER1, PER2, CRY1 and CRY2, which work with the help of transcriptional feedback loops. [41] These interlocked negative feedback loops are activated by Circadian Locomotor Output Cycles Kaput (CLOCK), Brain and Muscle ARNT-Like 1 (BMAL1) and ROR (retinoic acid receptor-related orphan receptor) and they are deactivated by cryptochrome (CRY), period (PER) and nuclear receptor 1D1/2, NR1D1/2 (REV-ERB). These

proteins form an independent transcriptional cell rhythm through which they conduct the circadian expression of a lot of target genes. [80]

CLOCK and BMAL1 are circadian transcription factors which bind to E-box elements and through heterodimerization and transactivation target genes like PER and CRY. Through the heterodimerization of PER and CRY they move to the nucleus where they stop the transcriptional activity of CLOCK:BMAL1. [41]

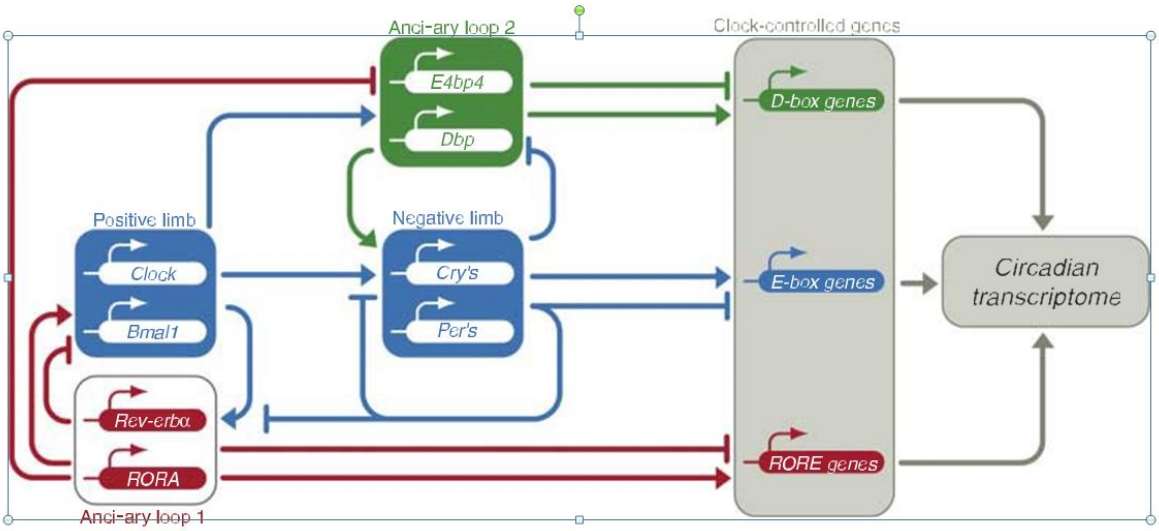


Fig.3 Feedback loops of the molecular oscillator and the main mechanism for coordinating circadian gene expression. The core oscillation depicted in blue lines is led by the positive limb of PER and CRY genes which have to be activated by CLOCK and BMAL and by the succeeding negative feedback of PER/CRY protein complex. These feedbacks are made possible with the help of sequences of CRY and PER genes through the E-box. The core is also sustained by a secondary loop depicted in red lines, which targets REV-ERB and RORA, who also have a rhythmical expression when there is an interaction of CLOCK/BMAL1 and PER/CRY proteins with the E-boxes. Then BMAL1 is led into expression of an anti-phase to PER and CRY genes with the involvement of REV-ERBA and RORA through RORE genes. There is another secondary mechanism with feedback into the core and it is marked by the green lines; it is also rhythmic and it consists of DBP/E4BP4; DBP which operates through the D-box genes, is led by inputs from the E-box and RORE genes. This system of circadian gene expression secures the oscillation of proteins in a definite sequence inside a cell, proteins which will time the expression of clock-led, output genes that contain E-Box, D-box and/ RORE sequences. Then the primary clock-led genes will control secondary ones and like this controlling the circadian trancriptome. [41]

Located in the heart, lungs, liver, skeletal muscle and adipose tissues are the peripheral circadian oscillators [41], which are synchronized to the SCN through neuronal signals and factors like glucocorticoids and insulin. [42]

Transcriptome-related research indicates that about 45% of mice transcripts show a circadian rhythm. [81] Among these genes are a lot of crucial regulators in the metabolic activity of glucose, lipids and oxidative phosphorylation. [82, 83]

Animal metabolism is furthermore influenced by feeding/fasting cycles. Circadian rhythms and feeding/fasting cycles coordinate genomic programs. [84] Feeding/fasting cycles influence key factors in the regulation of nutrient homeostasis like AMP-activated protein kinase (AMPK), cAMP response element-binding protein (CREB) and v-Akt murine thymoma viral oncogene homolog 1 (AKT/PKB); these factors also are linked to circadian proteins. Looking at kinase AMPK, we notice that it can phosphorylate CRY and therefore direct it to degrade; this becomes a way how fasting can impact the circadian clock. [85]

It appears that feeding/fasting cycles have an important effect on rhythmic hepatic gene expression. [86] One study investigated this by giving mice ad libitum access to food and it resulted in it mostly being consumed at night; a total of 3000 transcripts showed oscillation on a daily basis. But with no food intake, there were only 350 hepatic transcripts; this means that most hepatic transcripts that oscillate rhythmically during 24 hours are entrained by the daily rhythm of food intake. When mice were fed an isocaloric diet during daytime, there were 5000 hepatic transcripts with 24 hours rhythms and there was a change in the phase of oscillation for clock factors and other rhythmic transcripts. This suggests that timing of food consumption affects the phase of the circadian hepatic clock. When looking at mice with no CRY protein, they appear to have no daily feeding rhythm or hepatic oscillation of the transcript and with an isocaloric diet fed during the day, only 700 transcripts are recuperated. [86] These studies suggest that a working circadian clock, the presence of food and feeding timing play a key role in the functioning of the hepatic circadian transcriptome. [87]

Timing of food intake is the main influencing factor for the peripheral clock. [43]

Aiming to analyse the early impact of time-imposed restricted feeding (TRF) on behavioural and physiological parameters in animals, one study set six week old male C57BL/6J mice on a high-fat high-sucrose diet for one week. They were divided into two groups; one was fed during the sleep phase (DF) and the other during the active phase (NF). Both groups had access to a running wheel. The DF group showed 9% higher body weight than the NF mice and daily food intake was 10% higher in the DF group. When looking at the voluntary physical activity, the DF mice had a 34% lower activity than the NF group. When looking at the body temperature, the DF mice showed a rapid decline at midnight, going towards hypothermia and this was correlated to the decrease in physical exercise. On the other hand, the DF group had continuously higher levels of body temperature during the day than the NF mice, which indicated a poor sleep quality. Measures of corticosterone showed peak levels 1.8 times higher in the DG group compared to the NF, plasma insulin was 2.8 times higher

in the DF group and leptin 2.7 times higher than in the NF group, which suggests that DF induced leptin resistance, hyperinsulinemia and hypercorticosteronemia. Ghrelin levels were the same in both groups. Looking at gene expressions in the Hypothalamus linked to appetite, results show a 1.5 greater expression of orexigenic Neuropeptide Y (NPY) and a 2.2 higher expression of orexigenic agouti-related peptide (Agrp) in the DF mice compared to NF. And the mRNA of cocaine- and amphetamine-regulated transcript (Cartpt), which is an anorexigenic gene was 0.6 times lower in DF. DF mice also showed hepatic lipid accumulation and a higher lipogenic gene expression than NF mice. All these findings suggest that food intake at inappropriate time leads to obesity and metabolic dysfunction even after a short period of time. [44]

On the other hand, studies show that by giving mice access to food only at night, this can re-establish their natural feeding cycles and synchronize them with their circadian rhythms. [88] TRF has the potential to re-establish natural cycles of factors that control the metabolism, like cAMP response element-binding protein (CREB), mechanistic target of rapamycin (mTOR) and 5' AMP-activated protein kinase (AMPK) and also the circadian rhythms and therefore the expression of target genes, that are inhibited by diet-induced obesity. [89, 90, 91] The following figure depicts the impacts of TRF on the metabolism of mice.

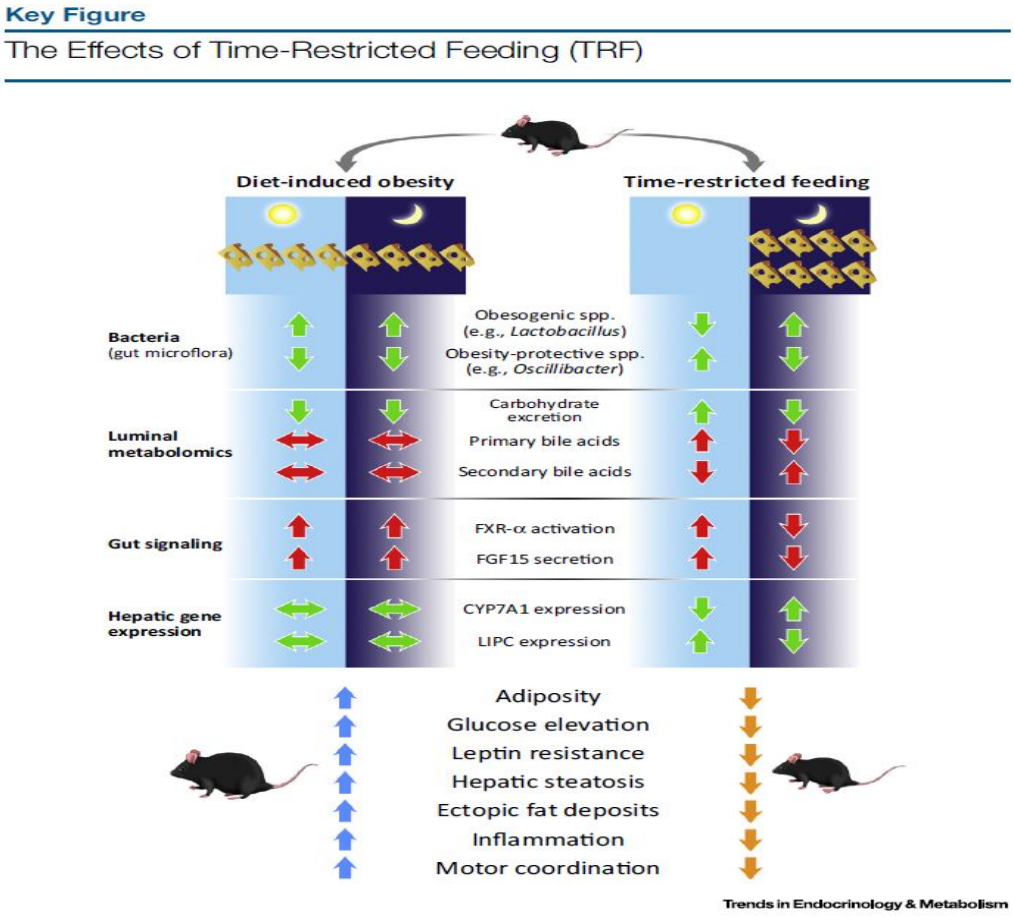


Fig.4 The impact of TRF on mice. Green arrows stand for conclusions from research and red arrows represent possible pathways. On the left we have effects on different parameters for mice, which had ad libitum access to a diet high in fat and on the right side we see the impact of TRF on the same parameters in mice. CYP7A1 = cytochrome P450 7A1; FGF15 = fibroblast growth factor 15; FXR = farnesoid X receptor; LIPC = hepatic lipase. [87]

Studies have shown that when feeding two groups of mice an isocaloric diet and putting them under a similar physical activity regime, mice which are on a TRF diet do not turn obese even with a diet high in fat. They are significantly less overweight than the ad libitum fed ones and they show better glucose and lipid metabolism, as well as less leptin resistance, hepatic inflammation and steatosis and ectopic lipid accumulation. They also show better motor coordination. [89, 90, 91]

Aiming to see if TRF can provide similar results in case of other obesogenic diets, like high-fructose or high-sucrose, a study used 392 twelve week old male wild-type C57BL/6J mice and subjected them to these diets for 12 weeks. One group of mice was fed ad libitum a high-fat, high-sucrose diet (ALF) and the other was fed the same diet including the same quantity of calories but within a time frame of 9 hours during the active phase of mice (TRF). Results showed that after the intervention period TRF mice had only a 21% increase in body weight compared to 42% increase of the ALF group. Also, TRF regime turned around the evolution of dysmetabolic effects in mice, which were obese prior to the intervention and which suffered from insulin resistance. The positive effects of TRF were directly proportional to the time frame of feeding, as the best results were achieved with 9 hours of TRF and then decreased with increasing time of food access (up to 15 hours). [92]

When looking at genetic causes of obesity and whether TRF can have a protective impact in this scenario, one study investigated PER1S714G mutated mice. These mice are prone to diet-induced obesity because their feeding rhythms are disturbed. The study showed that TRF was able to protect mice from weight increase under a high fat diet. [93]

2.2.1.6. Adverse effects of intermittent fasting

There are also some studies on rodents which show adverse effects of IF, like this study, which presented a better glucose tolerance after one month of ADF, but then it showed a decrease in glucose tolerance after 8 months of ADF, even though the ADF group showed a decrease in bodyweight compared to the ad libitum fed ones. The underlying mechanism of these results could not be found. [37]. Similar to this, adverse effects were also shown in another study, which concluded that IF had a negative impact on the glucose metabolism in low density lipopoprotein receptor deficient rats. [38] No other adverse effects were observed in the reviewed literature.

2.2.2. Impact of intermittent fasting on metabolic parameters and health in humans

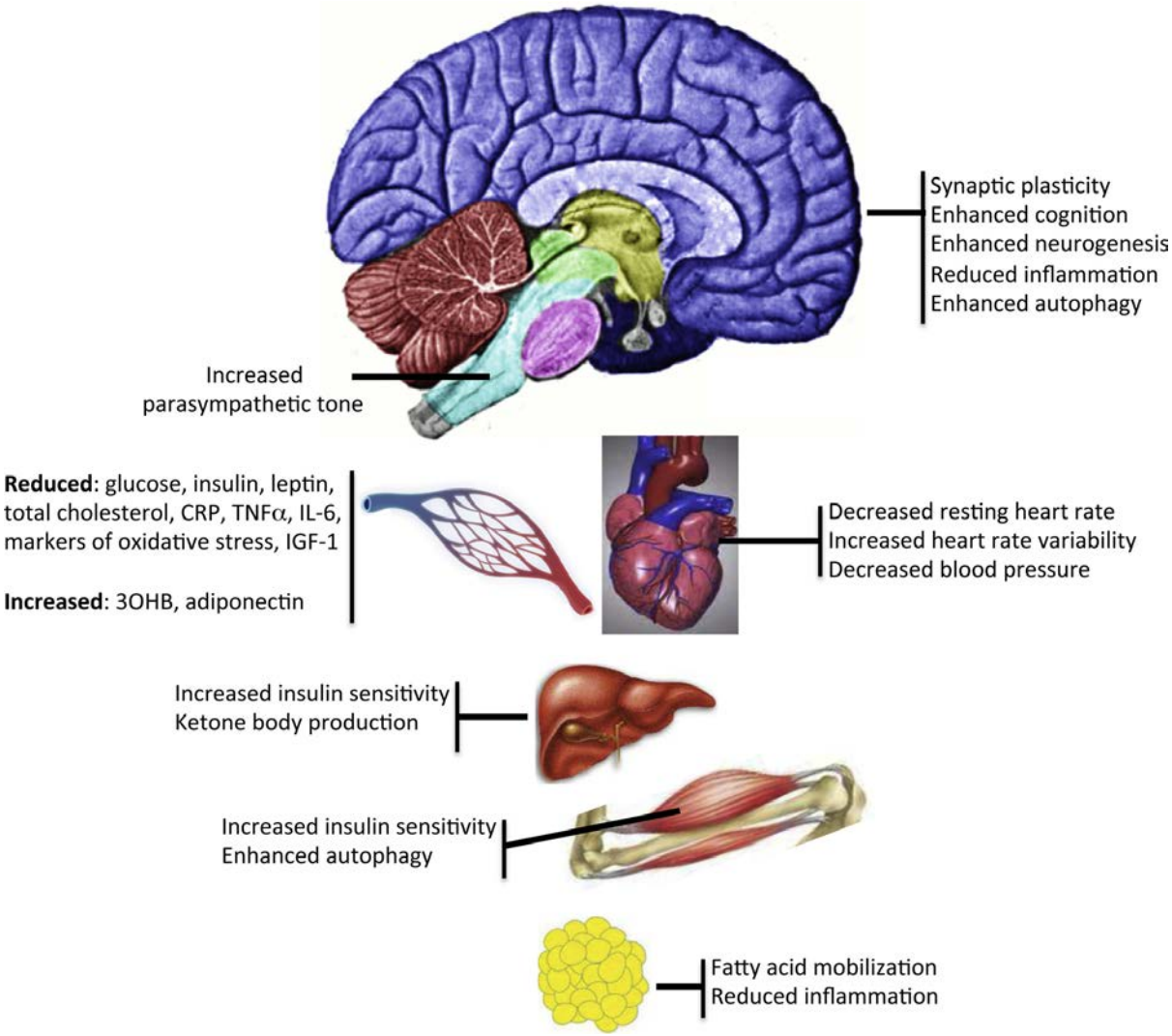


Fig. 5 Impact of intermittent fasting on different organs. 3OHB, 3-hydroxybutyrate; CRP, C-reactive protein; IGF-1, insulin-like growth factor 1; IL-6, interleukin 6; TNF-α, tumor necrosis factor α. [1]

Literature presents us with a series of impacts that IF produces in humans that are of paramount importance for maintaining or restoring health, like increases in synaptic plasticity, cognition, neurogenesis, autophagy and parasympathethic tone and decreases in inflammation, resting heart rate and blood pressure. Furthermore, it impacts the metabolism by reducing glucose, insulin, leptin, total cholesterol, CRP, TNFα, IL-6, IGF-1 and oxidative stress while at the same time raising 3OHB and adiponectin levels, insulin sensitivity, ketone production and fatty acid mobilization. [1]

2.2.2.1 Impact on body weight

To present an overview of the impact of IF on body weight in humans, a recent systematic review examined 27 trials focusing on weight loss in obese and overweight patients. It included 5:2 fasting, IF with a daily 16 hour fasting period and AD (alternate day fasting). In the non-fasting days some

studies allowed ad libitum food intake, while others restricted the calories. Also, on the fasting days, some studies allowed 25% of normal caloric intake, while others completely restricted the intake. 5 of the studies also included patients with type 2 diabetes. All participants in the 27 trials showed a decrease in body weight ranging from 0.8% to 13%. In twelve of the twenty-seven studies a calorie-restricted diet was used as a comparison and the results regarding weight loss were similar in both groups. The duration of the studies ranged from eight weeks to one year and the main way of decreasing body weight with IF was through fat loss. [45] Even though studies with interventions with duration of eight weeks to a year which had a follow-up period longer than six months showed regaining some body weight of the participants, the body weight was still significantly lower than the baseline. One of the longer interventions, which lasted a year, managed to show maintaining of the body weight of participants twelve months after the intervention ended. [46] When comparing IF and caloric restriction regarding the amount of regained weight, both showed similar results, even though one of the studies showed a different type of weight regain for IF compared to caloric restriction. The follow-up participants undergoing IF presented a regain of weight through lean body mass, whereas the calorie restricted group regained weight through both lean body mass and fat. [47]

2.2.2.2 Impact on metabolism

The first systematic review of clinical trials that assesses the impact of IF and CR on lipids in humans, like the low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triacylglycerols (TG) considered 28 publications with interventions with follow ups between 1-12 months. Participants were healthy or overweight/ obese individuals, or were suffering from non-alcoholic fatty liver disease, type 2 Diabetes or metabolic syndrome. Subgroup analyses were done for variables like sex, intervention type, health status, baseline levels of lipids and duration of the intervention.

Results show significant lower levels of LDL after IF and CR, both of the interventions causing a similar reduction. It has also been concluded that subjects with higher baseline LDL levels had a higher reduction in LDL-concentrations. LDL was only lower in subjects with a caloric intake restriction greater than 50% of their required daily energy intake. Only healthy participants showed a statistically significant decrease in LDL, while the reduction in non-healthy subjects was not statistically significant. Studies with exclusively female subjects experienced a greater decrease in LDL compared to mixed groups. When taking intervention time into consideration, studies showed similar results in the decrease of LDL independent whether they were carried out over or less than 8 weeks. HDL concentration didn't show any significant difference in the IF and CR interventions. Regarding TC, there was a significant lower concentration after CR but not after IF. It has also been concluded that participants with a greater TC baseline level had a higher reduction and that the decreases were noticed only in subjects consuming 50% or less of their required daily energy intake.

Also, greater reductions were noticed in studies with exclusively male subjects. When looking at TC, statistically significant reductions were only noticed in interventions with duration of more than 8 weeks and only in healthy subjects. [48] The underlying mechanism of the impact of IF on lipids is thought to be because of the nuclear expression of peroxisome proliferator-activated receptor-α and –g coactivator 1-α in the liver which causes higher fatty acid oxidation and Apolipoprotein A (ApoA) production, while lowering Apolipoprotein B (ApoB) production. Higher fatty acid oxidation comes with lower hepatic TG and low-density lipoprotein (VLDL) production. All this would cause a decrease in the concentrations of LDL and VLDL, which would cause a reduction in TC and TG levels.

It appears that during aging production of growth hormone (GH) and Insulin-like Growth Factor 1 (IGF-1) is starting to decrease. This process is called "somatopause" [49] and is associated with a reduction of bone and muscle mass, an increase in fat, dyslipidaemia, cardiovascular disease and cognitive degradation. [50.]. On the other hand, studies show that higher levels of circulating IGF-1 can be correlated to a greater risk of developing different cancer types , like prostate [51], colorectal [52] and premenopausal breast cancer [53]. Even though IFG-1 seems to have opposing effects on health and disease in humans, it is important to establish the variables which impact its bioactivity. A systematic review from 2019 analysed the impact of IF and CR on IGF-1 levels in healthy individuals. Ten studies including 497 participants have been selected for the review. The participants mean age was 36 years old and the average duration of the interventions was 20 weeks. When comparing IF and CR, results showed for IF a greater impact on lowering IFG-1 levels than CR. Since results for CR showed a lot of heterogeneity, it was divided into groups, where it appeared that restricting caloric consumption to 50% of normal daily recommended intake or less had a significantly greater reduction on IFG-1 than restricting to more than 50% of normal daily recommended intake. After conducting a dose-response analysis and a meta regression analysis for the caloric restricted regimes, it became obvious that the greater the caloric restriction, the less there was circulating IGF-1. [54]

2.2.2.3 Impact on diabetes type II

A systematic review from 2021 analysed the impact of IF on type 2 diabetes patients regarding body weight and glycaemic control. IF that were included were 24-hour complete fast, intermittent caloric restriction (25% of total caloric intake) and time restricted feeding (fasting for 16-20 hours a day). 7 studies were included with an intervention of an average duration of 24 weeks and with participants being on average 56 years old. The studies show a significant reduction in body weight compared to

the control groups. Regarding HbA1c there was no significant decrease in the IF arm compared to control. [45]

On the other hand, a randomized control trial analysing the impact of TRF on pre-diabetic men succeeded in presenting better insulin levels, improved insulin sensitivity and β cell responsiveness after 5 weeks of intervention, in which they ate an iso- and eucaloric diet within a 6-hour timeframe, with the last meal being at 3 pm compared to the control group, which ate between 8 am and 8 pm [58] which indicates that improvement of diabetes risk markers is possible even without weight loss.

Another clinical trial was conducted with overweight women with ages between 29 and 69 years old. They were assigned to either an intermittent energy and carbohydrate restriction group (IECR) with 25% overall caloric restriction and 2 fasting days per week (2500–2717 kJ/d for fasting days) or a daily energy restricted group with an overall energy restriction of 25% and a mediterranean diet (DER) daily (6000 kJ/d). There was also a third group, which was a IECR group but with unlimited access to protein and fat (IECR + PF for a day/week). The intervention went over 4 months and the results showed a significantly greater decrease in serum insulin and HOMA for the IECR groups in comparison to DER, but there was no significant difference in HbA1c between groups. Also, the IECR groups had a significant decrease in body fat compared to the DER arm. [100]

2.2.2.4 Impact on inflammation

A systematic review focusing on clinical studies that investigated the impact of IF on plasma concentrations of inflammatory biomarkers narrowed down the available evidence on this subject to 15 eligible studies. It includes patients with ages 23 to 58 that are healthy or that suffer from sleep apnea, rheumatoid arthritis and overweight/obesity. It showed a statistically significant decrease in C - reactive protein (CRP) both with IF and with CR. But when comparing the two intervention types, IF was more effective in decreasing CRP than CR. A higher decrease was shown in interventions of 8 weeks or longer and in overweight/obese individuals. When looking at TNF-α and IL-6 levels, IF and CR showed no statistically significant impact on these markers. [55]

2.2.2.5 Impact of time-imposed restricted feeding and the mechanism of the circadian biology in humans

While positive impacts of some forms of IF may come partially or entirely from caloric reduction [56], there is one type of IF which shows a positive influence on the health of both animals [57] and humans [58, 59] regardless of caloric restriction and it's called TRF. TRF refers to fasting for at least 14 hours a day and excludes Ramadan fasting. When looking at the 9 TRF trials in humans conducted until

2019 [58, 59, 60–66], benefits like losing weight and decreased insulin levels, better insulin sensitivity and blood pressure appeared in those trials, where the subjects consumed food in the morning or at midday [58, 59, 60–64], whereas the studies where participants ate later in the day showed zero effects or even worse cardio-metabolic parameters. [65–67]. These time-related differences may be explained by the circadian rhythm. To better understand this, we need to take a closer look at the mechanism of the circadian biology.

Circadian rhythms are produced endogenously in the organism and continue to function also in the absence of time cues that come from outside. Evolving over hundreds of millions of years, they are meant to regulate the metabolism so that processes like anabolism and catabolism which are opposite in effect are differentiated by time and in order to foresee feeding-fasting cycles for better metabolic efficiency. [68]

There are two elements in the circadian system, one being the central clock, seated in the SCN and the second component being a number of peripheral clocks located in all other tissues of the body. The central clock operates mainly through cortisol and melatonin and synaptic projections. [69]

Peripheral clocks receive cues from the central clock alongside environmental and behavioural factors and also their own rhythms in order to control metabolic activity rhythmically. [70]

Inside the cells, autonomous rhythms are sustained molecularly with the help of clock genes and proteins that build a transcriptional-translational feedback loop (TTFL), which acts in a 24h rhythm. [71]

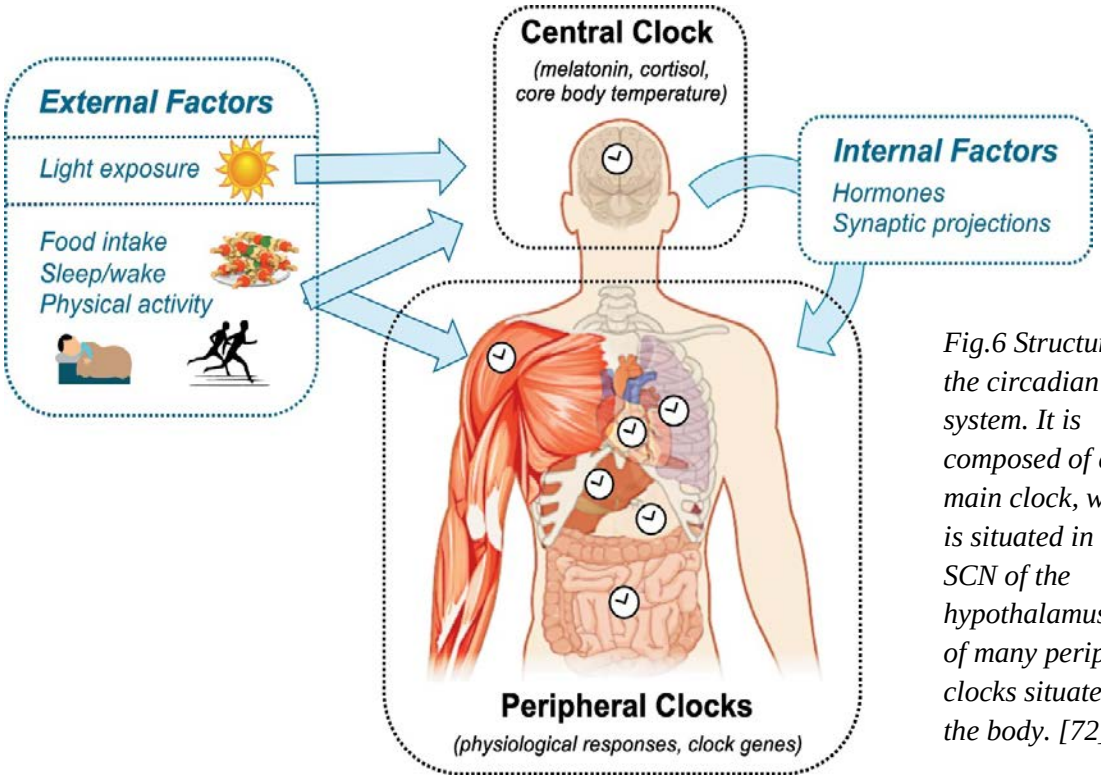


Fig.6 Structure of the circadian clock system. It is composed of a main clock, which is situated in the SCN of the hypothalamus and of many peripheral clocks situated in the body. [72]

While the central clock is entrained by light, the peripheral clocks receive cues from the central clock but also from external factors like light, exercise, food intake, sleep and metabolites. [69, 70] In the light of recent findings, one of these factors appears to be of most importance, namely the timing of food intake. [73]

If the zeitgebers of these two clock systems are not synchronized, this will negatively impact the metabolism, which can cause metabolic diseases. [72]

Studies investigating circadian variation in glucose metabolism found that **glucose tolerance** shows **circadian rhythm**, with lower glycemic control in the evening and at night for healthy subjects. On the other hand, glycemic control and diurnal rhythms like peripheral insulin sensitivity show a delay in phase for obese and type 2 diabetes patients; this indicates that delayed circadian rhythms could be either a cause or an effect for metabolic diseases.

When looking at **lipids**, they appear to be the most influenced plasma metabolites by the circadian clock, [74] with phases peaking in the morning and midday but they also present a large variability among different individuals. To better understand the type and degree of this variability, further controlled trials are needed. [72]

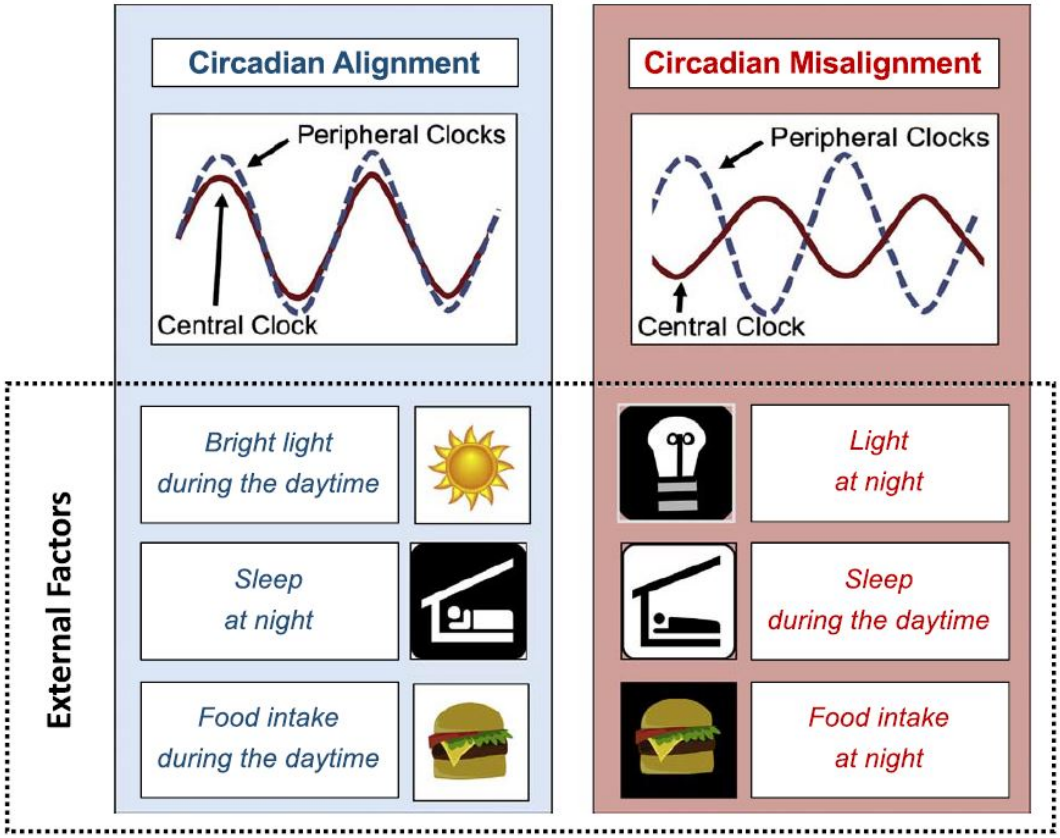


Fig.7 This figure shows how external factors like exposing to bright light and food consumption during the day and sleeping at night will align the central and peripheral circadian clocks (left), whereas bright lights or food consumption during night time or sleep during the day will misalign the two circadian clocks (right). [72]

Studies investigating the **impact of delayed food intake** even if it's during daytime show that this has a negative impact on metabolism. One study looked at the consequences of shifting lunch intake from 1 pm to 4.30 pm for seven days. Results showed an increase of 46% in glucose (AUC) and a decrease in fasting energy expenditure of 4%. [75] Another study wanted to evaluate the impact of a single load of late evening meal and therefore moved dinner time from 7 pm to 10.30 pm. Results showed a 7-8 % increase in the 5 hour glucose AUC right after the meal but also after the breakfast on the next day, with an overall increase of 4% in the 24h glucose. [76]

Regarding **caloric distribution during a day**, a randomized control trial compared body weight differences in overweight women eating most of their calories during early hours versus later in the day. They concluded that those who consumed 70% of their total calories from a day before 12 pm

had a 0.6 kg decrease in body weight after the intervention period of six weeks compared to those which ate them after 4.30 pm. [77]
Another study comparing 420 early and late eaters was conducted over 20 weeks on female subjects with a mean age of 42 years and a BMI of about 31.4 showed that early eaters (lunch before 3 pm) had a 2 % greater decrease in body weight than late eaters, even though they had the same self-reported food intake, energy expenditure and sleep. [78]
Another RCT conducted over 12 weeks compared weight loss in overweight and obese women by grouping them into two categories, B-group that ate 700 kcal at breakfast, 500kcal for lunch and 200 kcal at dinner and D-group, which had 200 kcal for breakfast, 500 kcal for lunch and 700 kcal for dinner. Both groups showed a significant lower body weight after the intervention, but the B-group presented a 2.5 higher weight loss than the D-group. Serum **triglycerides** were 33.6% lower than baseline in the B-group, while in the D-group they were 14.6% more elevated than baseline. Total **cholesterol** was significantly decreased only in the B-group and HDL-cholesterol was significantly higher also only in the B-group. Regarding fasting parameters like **glucose, ghrelin and insulin** levels they were decreased in both groups, yet the reduction was greater in the B-group. [79]

Despite the amount of evidence of the positive impacts of TRF, its molecular mechanism is still unclear. The first clinical trial to investigate the consequences of TRF on gene expression and diurnal rhythms in risk factors for cadiometabolic diseases in humans was conducted in 2019 and it was only the second trial to focus on early TRF (eTRF). Participants were healthy individuals 20 – 45 years old with a BMI ranging from 25 – 35 kg/m2, regular sleeping hours between 21.30 and 24.00. They were divided into two groups, the control group which ate between 8.00 and 20.00 and the eTRF group which restricted their feeding time to 8.00 until 14.00 for a period of four days. There was a cross-over to the other group after about 4 weeks. Regarding glycemic markers, results showed a significant decrease in mean-24 h glucose levels for the eTRF group. Also, fasting glucose and insulin levels in the morning were significantly decreased in the eTRF group and therefore HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was also significantly lower. IRS2 (Insulin Receptor Substrate 2) gene expression was significantly increased. In the evening, results in the eTRF group show a significant decrease of fasting insulin and HOMA-IR, while glucose levels showed no change. And AKT2 gene expression was significantly higher in the eTRF arm. [94]

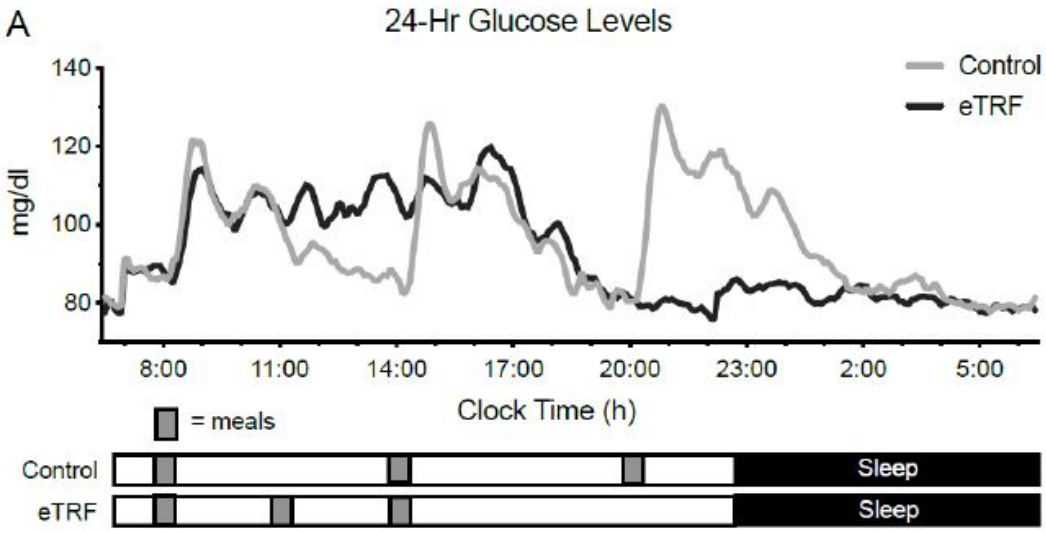


Fig. 8 24-h glucose levels in the control group and the eTRF group measured through continuous glucose monitoring. [94]

Regarding lipids, the eTRF arm showed higher LDL and HDL cholesterol in the morning with no differences in triglycerides or free fatty acids. Hydroxybutyrate was also significantly increased by eTRF in the morning. Yet in the evening there were no significant differences in lipid levels between groups.

When looking at **gene expression of circadian clock genes** in the eTRF group, they were significantly higher in the morning for BMAL1, CRY1, CRY2 and RORA, whereas in the evening they were significantly lower for PER1 and slightly higher in CRY1, CRY2, REV-ERBA and RORA, while CLOCK and PER2 remained unchanged. eTRF caused the longevity genes Sirtuin-1 (SIRT1) to be higher in the morning and MTOR to be higher in the evening. And the autophagy gene LC3A was significantly higher both in the morning and evening.

Another clinical trial set out to determine the effects of eTRF over a period of 5 weeks within a randomized, crossover trial with an isocaloric and eucaloric diet in prediabetic men. The eTRF group was given a 6 hour feeding time frame with the last meal in the day at 3 pm versus the control group which had a feeding timeframe of 12 hours, from 8 am to 8 pm. The study achieved to become the most strictly controlled IF trial in humans up to 2018. Results after 5 weeks showed improved insulin levels for the eTRF group, better insulin sensitivity and β cell responsiveness, lower blood pressure and oxidative stress values. And this was possible even without any weight loss of the participants,

which indicates that combining an IF regime with the rhythms of the biological clocks can lead to very promising results in regard to cardiometabolic health in humans. [58]

2.2.2.6 Adverse effects

A systematic review assessing the effects of IF on overweight and obese subjects didn't find any report of a serious adverse event. Mood-related issues and side-effects like binge-eating would be expected but have not occurred during these interventions. On the contrary, participants declared to have better mood, a better body image and a decrease in depression. [45]

A clinical trial from 2018 that conducted an intervention of eTRF over a period of 5 weeks reported some minor adverse events, like a case of vomiting, one of frequent urination and of feeling tired, headaches, an increased sense of thirst and diarrhoea, but no serious adverse events. [58]

No other adverse effects were observed in the reviewed literature.

3. MATERIAL AND METHODS

Literature research shows promising results regarding intermittent fasting as a potential preventive or therapeutic method for global diseases of public health concern, like cardiovascular diseases, cognitive disorders and diabetes. Furthermore, the mechanism of the circadian rhythm is being explored, alongside its impact on risk factors for these global burdens of disease. Clinical trials and systematic reviews of clinical trials on animals and humans have been included. The aim of this master thesis is to conclude whether intermittent fasting and eating behaviours aligned with the circadian rhythm show the positive impacts on health found in clinical trials also in day by day life of people when randomly selected and questioned.

3.1 Study design

In order to test the hypotheses of this study an online survey was established consisting of 47 questions divided into six categories - lifestyle, health condition, sleep, cognitive abilities, nutrition and personal information. The first category, lifestyle includes questions about physical activity, smoking status, alcohol intake and quality of life. Health condition was assessed through a subjective evaluation of the personal state of health and through questions about existing risk factors or diseases. Also, participants were asked if they undergo an annual health check and whether they were taking any medication. The sleep category consists of assessing if the subjects have regular sleeping times, how well-rested they wake up in the morning and whether they sometimes have night shifts and if so, how often. The cognitive abilities were established through a subjective evaluation of each participant, by answering whether they feel like they are often forgetful and how fast they learn new information, and also through a more objective means of evaluation, by answering three questions inspired from an online cognitive ability test. These questions had a time limit of 60 to 90 seconds, which was established by taking a subsample of 10 people and asking them to solve those problems as fast as possible and then calculating a mean completion time for each of the three questions. The nutrition section consisted of questions regarding particular diets of the participants, how many times a day they have food intake, what time the last meal is in a day, what time do they have their main meal and if and when they have breakfast, lunch and dinner during the week and in the weekends. The platform limesurvey was used to host this questionnaire and after testing it regarding clarity of the questions and the structure on a small group of people, it was published on the 2nd of December 2020 in German language and on the 6th of May 2021 an English version was also published in order to reach a larger group of people. Social media platforms were used to spread the survey and to reach people that practice intermittent fasting, have different diets but also to reach people that don't do intermittent fasting or that have a particular interest in nutrition. Both surveys were terminated on 11th of March 2022.

3.2 Study population

The survey was designed for participants of ages between 18 and 65 years old. This was assessed through the personal details section by asking them to state their current age. As the survey was presented in two languages, German and English, it was meant to reach a large group of people living in different European or other international countries.

3.3 Survey tool

The survey was based on two hypotheses that are presented below. Lifestyle of the subjects was assessed by asking if and how often they exercise, what type of exercise or sport they practice, if they use a step counter and if so how many steps a day they walk on average, their past and current smoking status, if and how much alcohol they consume and on a scale of one to ten how they appreciate their quality of life (“1” representing “very good” and “10” “very poor”). Their health condition was assessed through a self-evaluation question that included the options “very good”, “good”, “bad” and “very bad”. Regarding health, they were also asked to answer whether they undergo an annual health check and if any risk factors (high blood pressure, high blood lipids, high blood sugar level, etc.) or chronic diseases had been detected. If so, they were asked to state exactly what risk factor or disease had been detected. Furthermore, they had to state whether they are currently taking any medication and if so, which medication. Sleep-related data was assessed by asking if they have regular sleeping times and if so, what the sleeping and wake-up times are. They were also asked whether they sometimes have night shifts and if so, how often in a month. Lastly they were asked to state on a scale from one to ten how well rested they wake up (“1” being “very well rested” and “10” being “very tired”). Cognition was assessed by asking the participants to estimate how fast they learn new information, possible answers including “very fast”, “average” and “very difficult”. Furthermore, they were asked if they are often forgetful (“yes”, “no”, “sometimes”). To further assess their cognitive abilities, they were asked to solve the following exercises. The first exercise stated that there are 420 people in a room, 172 that understand English and 122 that understand German. The question was what percentage of the people does understand neither English nor German. This question had a completion time limit of 90 seconds. The second exercise stated that all children in a classroom receive sweets. And that a lot of the colourful packed sweets also contain a surprise. Kathy didn't receive any surprise when she opened her sweet. Conclusion: Kathy has received a colourful packed sweet that didn't contain any surprise. The question was whether the conclusion is true, false or cannot be determined with the provided information. For this exercise the completion time limit was 60 seconds. The third cognition exercise stated that 9 cats in a shelter have the same numbers of toys. The dogs have 153 toys. Dogs and cats have together 234 toys. The question was how many toys each cat has. Completion time limit for this question was also 60 seconds. Nutrition-related data was assessed by asking the subjects if they have a specific type of diet and if so the possible answers included vegetarian (no meat & fish, but milk products and/or eggs), pescetarian (no meat, but fish and/or milk

products and/or eggs), vegan (no animal products), ketogenic (low carb), paleo (stone age diet), raw, IF (how many hours a day and/or how many days in a week?) and other. Further questions regarding dietary habits included how many meals they would eat on average in a day, what time they consume their last meal, what time they consume their main meal, if and at what time they consume breakfast, lunch and dinner during the week and on the weekends. Lastly, they were asked to complete general information, including gender, age, height, weight and occupation.

3.3.1. Hypothesis 1

"Intermittent fasting has a positive impact on body weight, metabolic and cardio-metabolic parameters like glucose levels, insulin sensitivity, lipids and blood pressure, quality of life and cognitive abilities."

3.3.2. Hypothesis 2

"Food intake outside of the circadian rhythm has a negative impact on body weight, cardio-metabolic parameters, sleep quality, quality of life and cognitive abilities."

3.3.3 Statistics

The statistical evaluation of the data was carried out using SPSS 20.00 for Windows. The significance level was set at $p \leq .05$. Data from both the English version and the German version of the online survey were uploaded into a single data file on 16th of March and was then statistically analysed to present the results as follows.

4. RESULTS AND DISCUSSION

4.1 Descriptive results

Extent of the study and general characterization of the study participants

In total there were 203 participants that completed the online survey completely, out of which 173 were female participants and 30 male participants. Overall the mean age of the participants was 37.09 (Std. Dev. ± 10.67) years and the mean BMI was 26.42 (Std. Dev. ± 8.18).

Characterization of the study participants by age, height, weight and BMI

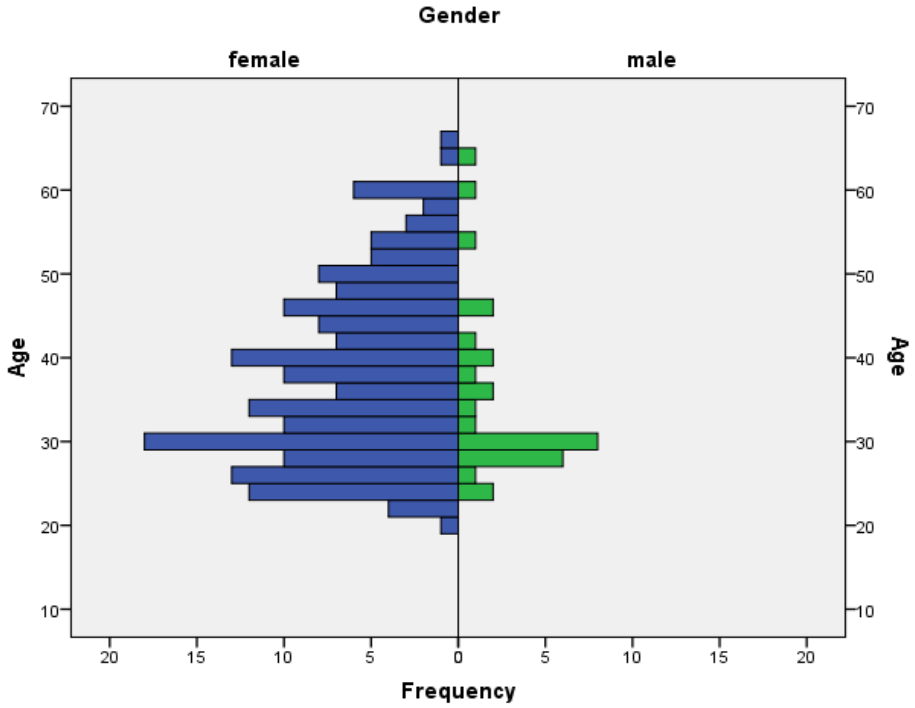


Fig. 9 Population pyramid of the participants.

	Female			Male			Total		
	N	Mean	Std.-Dev.	N	Mean	Std.-Dev.	N	Mean	Std.-Dev.
Age	173	37.53	10.70	30	34.57	10.28	203	37.09	10.67
Height (m)	173	1.67	0.06	30	1.80	0.06	203	1.69	0.08
Weight (kg)	173	73.81	23.71	30	84.30	24.00	203	75.36	23.99
BMI	173	26.49	8.37	30	26.01	7.10	203	26.42	8.18

Table 1 Characterization of the study participants by age, height, weight and BMI. N: number; Std. Dev.: Standard Deviation

Even though the male subjects had a lower mean age than the female participants, the difference between the two groups is not statistically relevant.

BMI of the participants

The mean BMI of the participants was 26.42 (Std. Dev. ± 8.18). When taking into consideration the age categories, we can observe an increase in the mean BMI with increasing age category. The mean BMI for the age group 18 – 30 being 23.84 (Std. Dev. ± 5.51), the mean BMI for the age group 31 – 45 being 26.36 (Std. Dev. ± 7.61) and the mean BMI for the third age category (46 – 65 years) being 31.03 (Std. Dev. ± 10.91). There are statistically relevant differences regarding BMI between the youngest and the middle aged group ($p = 0.02$) and between the youngest and the oldest group category ($p = 0.00$). There were no statistically relevant differences in the mean BMI between the female and the male subjects.

The distribution of the BMI deviates considerably from a normal distribution, but we can still notice a tendency for a right skewing like shown in the figure below.

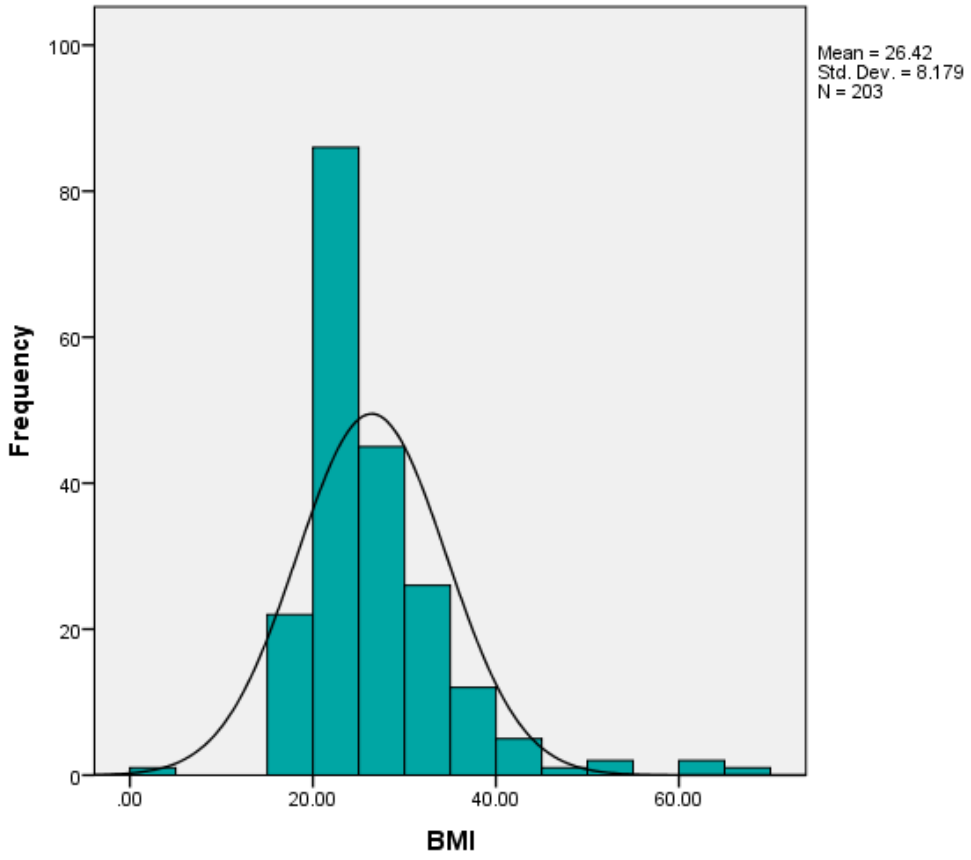
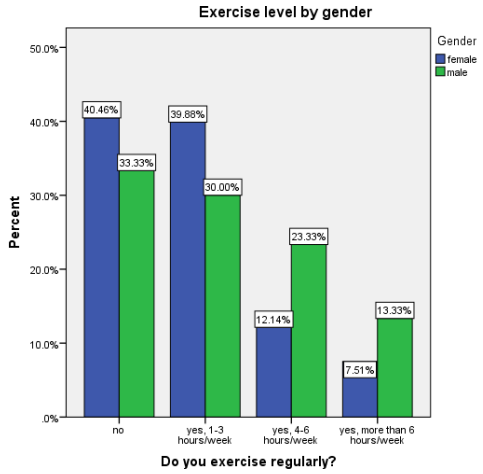


Fig. 10 Histogram of the BMI of the participants.

Characterization of the participants for exercise status and health condition

a)



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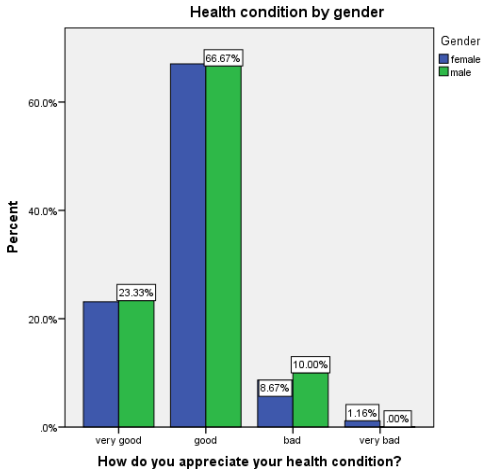
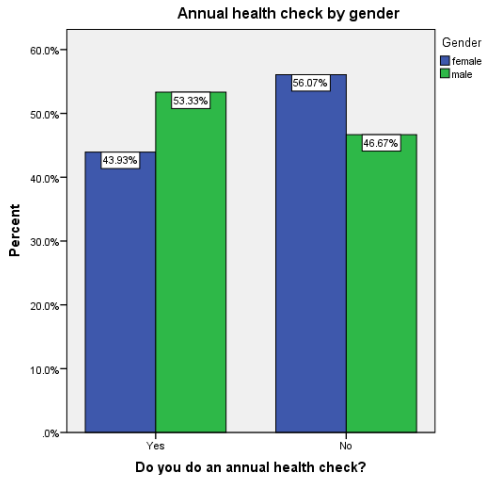


c)



d)

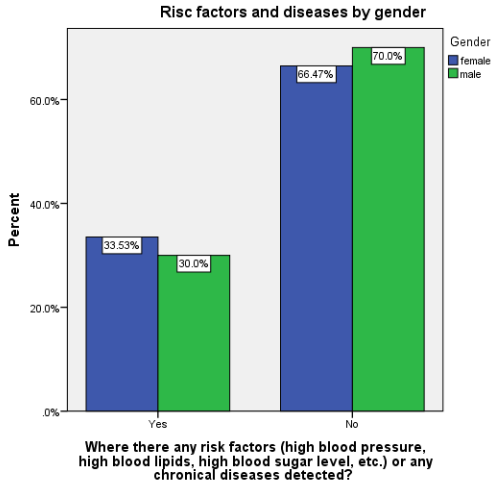


Fig. 11 Characterization of the participants by gender for a) exercise level; b) health condition; c) annual health check; d) detected risk factors

40.46% of the female participants and 33.33% of the male participants have declared that they don't exercise regularly. On the other hand, about 39.88% of women and 30% of men do exercise at least 1 -

3 hours per week, thus following the WHO recommendation for adults between 18 – 65 years old of doing sweaty exercise such as jogging or walking for 75 – 150 minutes every week. About 66.7% of the participants, both female and male likewise, appreciate their health condition to be good, while 23.3% evaluate it to be very good. 53.3% of men undertake a yearly health check, while only 44% of women check their health status annually. When looking at known risk factors such as high blood pressure, high blood lipids, high blood sugar or any other chronic disease, 30% of the men and 33.5% of the women have declared to suffer from at least one of them.

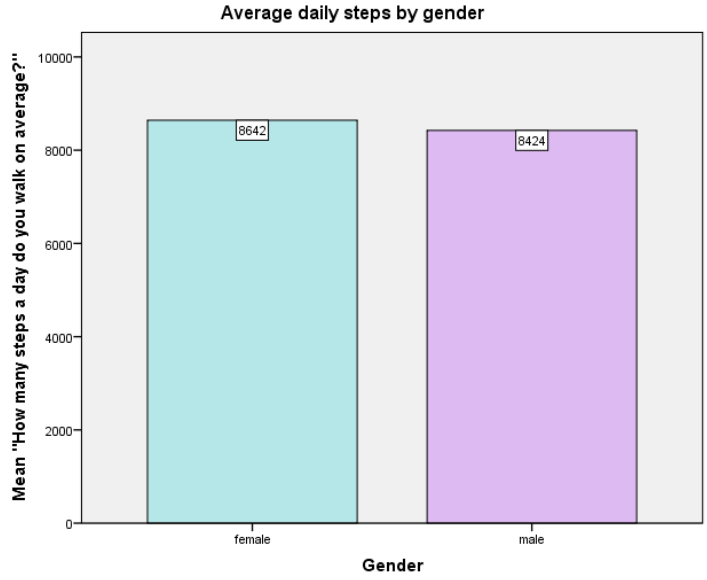


Fig. 12 Average daily step count by gender.

54.7 % of all subjects have declared they use a step counter. On average women walk about 8642 steps a day and men about 8424.

Characterization of the participants by risk factors and diseases

33% of the subjects have declared to suffer from at least one risk factor or disease. High blood pressure was the most common risk factor with 11.3% of the subjects suffering from it, women having a slightly higher percentage than men, with 11.6% for women and 10% for men. High blood lipids were the second most common risk factor, in total 8.9% suffering from it. Here, the women seem to have a much higher rate than men, with 6.9% vs. 2% of men declaring to have high blood lipids. The third place is occupied by high fasting glucose or high HbA1c. 6.4% of the sample presents this risk factor out of which 5.4% is represented by females and only 1% by men. 4.4% of the subjects have been diagnosed with diabetes type II, out of which 3.9% are women and 0.5% men. Heart attack and stroke have each occurred only in 0.5% of the subjects and the rest of 14.3 % represents other risk factor or diseases.

Where there any risk factors (high blood pressure, high blood lipids, high blood sugar level, etc.) or any chronic diseases detected?

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	67	33.0	33.0	33.0
	No	136	67.0	67.0	100.0
	Total	203	100.0	100.0	

Table 2 Risk factors and diseases.

Risk factors and diseases		Gender		Total
		female	male	
High blood pressure	Count	20	3	23
	Percent within gender	11.6%	10.0%	
	Percent of total population	9.9%	1.5%	11.3%
High blood lipids	Count	14	4	42
	Percent within gender	8.1%	13.3%	
	Percent of total population	6.9%	2.0%	8.9%
High fasting glucose or high HbA1c	Count	11	2	13
	Percent within gender	6.4%	6.7%	
	Percent of total population	5.4%	1.0%	6.4%
Diabetes type II	Count	8	1	9
	Percent within gender	4.6%	3.3%	
	Percent of total population	3.9%	0.5%	4.4%
Heart attack	Count	0	1	1
	Percent within gender	0.0%	3.3%	
	Percent of total population	0.0%	0.5%	0.5%
Stroke	Count	0	1	1
	Percent within gender	0.0%	3.3%	
	Percent of total population	0.0%	0.5%	0.5%
Other	Count	28	1	29

	Percent within gender	16.2%	3.3%	
	Percent of total population	13.8%	0.5%	14.3%
Total	Count	173	30	203
	Percent of total population	85.2%	14.8%	100%

Table 3 Cross-tabulation of risk factors and diseases of the subjects with gender.

Characterization of the participants by type of their diet

As we can observe in figure 13, more than half of the participants (54.68%) have a mixed type of diet, meaning that they consume both animal and vegetable products. The second biggest category is represented by those who declare to practice intermittent fasting, which are 22.66% of all participants. Vegetarians are represented by 8.38%, pescetarians by 5.42% and adapts of a ketogenic diet represent about 4.93% of the participants. Other types of diet such as vegan, raw and paleo are found less in than 5 % of the participants.

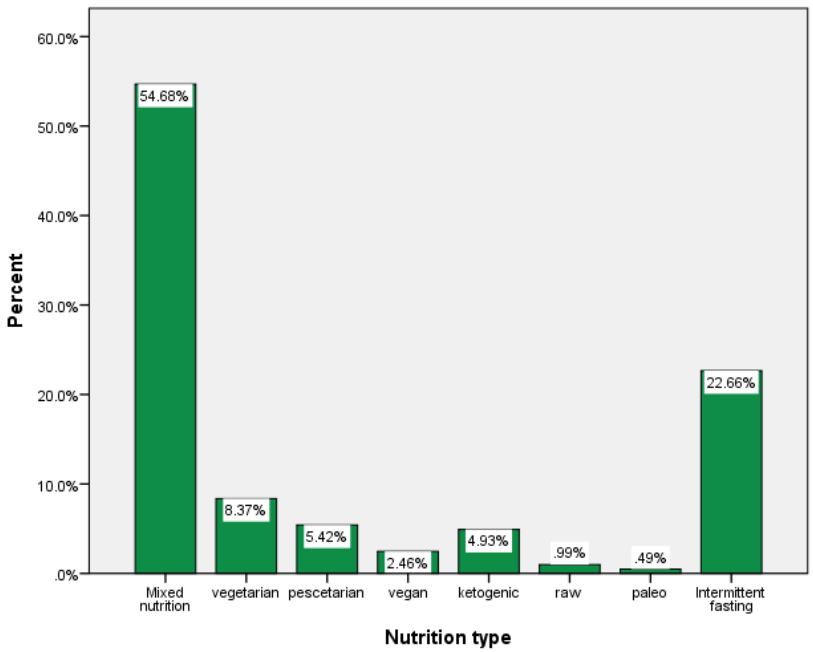
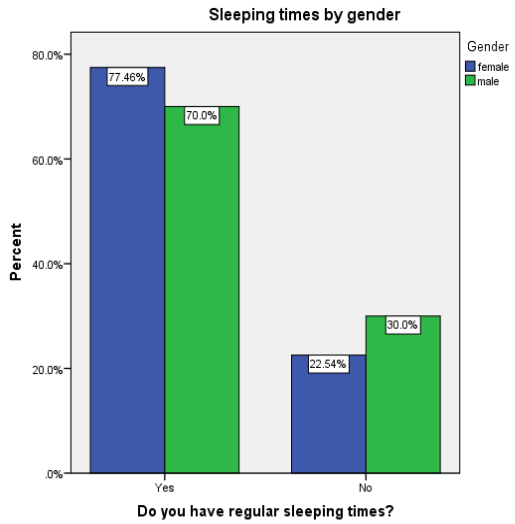


Fig. 13 Diet of the subjects

Characterization of the participants by sleeping times and night shifts



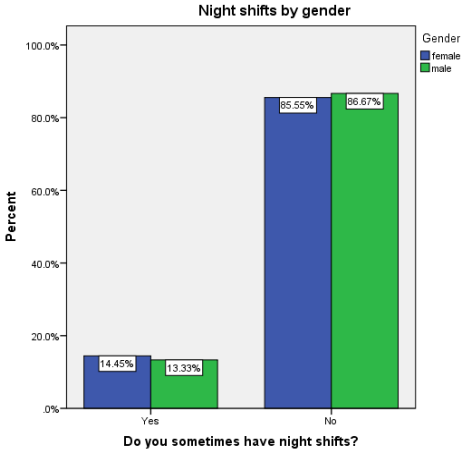


Fig. 14 Sleeping times of the subjects by gender

Fig. 15 Night shifts of the subjects by gender

When looking at sleeping schedules, 70% of men and 77.5% of women declared to have regular sleeping times and only 13.3% of men and 14.5% of women said that they had night shifts at least once a month.

Characterization of the participants by occupation

93.8% of the subjects in the age category 31 – 45 are actively working. Over 20% of the participants in the age category 18 – 30 are studying and over 20% of the 46 to 65 years old participants are unemployed.

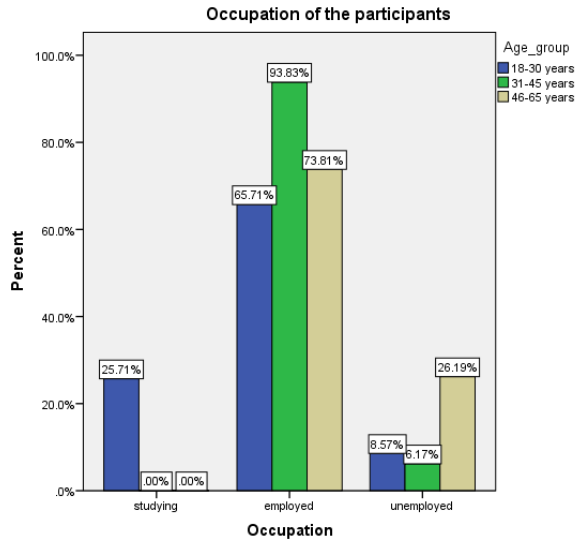


Fig. 16 Occupation category of the participants by age group.

4.2 RESULTS AND DISCUSSION

In order to test the two hypotheses of this paper the different statistical methods were used as follows. To calculate differences in mean values between two groups, the t-test for independent samples was used. The necessary requirements for the use of the t-test were checked beforehand. These are the interval scale level, the normal distribution of the data, respectively a group size greater than 30 participants and the homogeneity of variances. The Levene-test was used to check for the homogeneity of variances. If the results are significant, the heterogeneous variances have to be taken into account, which is why the testing of the hypothesis was done via a modified t-test.
If the requirements for the t-test were not met, then the Mann-Whitney-U-test was used instead.
For calculating with nominal variables the chi-quadrat-test for independence with a cross-table was used. This test is used to check whether two or more variables are statistically independent from each other.

Hypotheses

On the next few pages, the hypotheses are examined and the results described. For a better overview, the results are also presented in tabular form.

Results and discussion hypothesis 1

"Intermittent fasting has a positive impact on body weight, metabolic and cardio-metabolic parameters like glucose levels, insulin sensitivity, lipids and blood pressure, quality of life and cognitive abilities."

In order to define the variable "IF Group" (intermittent fasting group), the interval between the subject's chosen time for "breakfast" during the week and "time of the last meal" during the week was used. If no breakfast was eaten, the interval between "noon" and "time of the last meal" during the week was taken into account. In addition, the subjects that declared to practice "intermittent fasting" were included. In the case of 2 people, it was not possible to assign them to the IF Group and Non-IF Group because no precise meal times were given. These 2 cases were counted as missing.

In the following, the frequencies of the independent variable used "IF Group" is to be listed as an overview (see Table 4). The variable is then analysed using the t-test, U-test and chi-square test. The calculations are shown for the total sample, as well as separately according to gender, and for females also separately according to age groups.

	Total sample		Female		Male		18-30 years (female)		31-45 years (female)		46-65 years (female)	
	N	**%**	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**
IF Group	93	45.8	87	50.3	6	20.0	26	44.8	37	49.3	24	60.0
non-IF Group	108	53.2	84	48.6	24	80.0	32	55.2	37	49.3	15	37.5

Table 4 Frequencies for IF-Group. IF-Group mean age: 38.55 years (Std. Dev. ± 11.11); non-IF Group mean age: 35.23 years (Std. Dev. ± 9.93).

45.8% of the subjects were attributed to the IF-Group. From the female population, 50.3% were practicing IF and from the males 20%. When looking at the different age categories for the female subjects, we can notice an ascendant trend in intermittent fasting with growing age.

When analysing the possible impact of IF regarding BMI and quality of life of the participants, the results of the t-test show no significant group difference with regard to BMI or quality of life (see Table 5).

		IF Group	***N***	**Mean**	**Std. Deviation**	***p***
Total sample	BMI	IF Group	93	27.12	9.19	0.27
		non-IF Group	108	25.84	7.26	
	Quality of life	IF Group	93	3.68	2.22	0.92
		non-IF Group	108	3.65	2.04	
Female	BMI	IF Group	87	26.95	9.00	0.49
		non-IF Group	84	26.06	7.77	
	Quality of life	IF Group	87	3.68	2.24	0.95
		non-IF Group	84	3.65	2.22	
Male	BMI	IF Group	6	29.68	12.30	0.41
		non-IF Group	24	25.10	5.13	
	Quality of life	IF Group	6	3.67	2.16	0.95
		non-IF Group	24	3.63	1.28	
18-30 years (female)	BMI	IF Group	26	24.56	6.65	0.35
		non-IF Group	32	23.10	5.24	

	Quality of life	IF Group	26	3.88	2.12	0.49
		non-IF Group	32	3.50	2.11	
31-45 years (female)	BMI	IF Group	37	26.09	4.68	0.80
		non-IF Group	37	26.54	9.30	
	Quality of life	IF Group	37	3.70	2.36	0.80
		non-IF Group	37	3.57	1.86	
46-65 years (female)	BMI	IF Group	24	30.85	14.03	0.93
		non-IF Group	15	31.18	5.12	
	Quality of life	IF Group	24	3.42	2.24	0.37
		non-IF Group	15	4.20	3.17	

Table 5 Results of the t-test for hypothesis 1 regarding BMI and quality of life

The results of the U-test, shown in Table 6, show a significant group difference with regard to how fast the participants declare to learn new information and how forgetful they declare they are. In regard to how fast the subjects learn new information, the IF-Group shows a significantly lower mean rank than the non-IF group in the total sample and the female sample, which means that they have a faster learning ability. Regarding forgetfulness, again in the total sample and the female sample there is a significantly higher mean rank than the non-IF group, which means the IF Group is less forgetful. On the other hand, when looking at the subjective appreciation of their own health condition, the female IF group aged between 18 – 30 years shows a significantly higher middle ranking which stands for a poorer state of health.

		IF Group	***N***	**Mean Rank**	***p*** ***d****
Total sample	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 –	IF Group	93	91.73	**0.02** d=0.30
		non-IF Group	108	108.98	

	„difficult“)				
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	93	112.32	**.005** d=0.37
		non-IF Group	108	91.25	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	IF Group	93	106.39	0.12
		non-IF Group	108	96.36	
Female	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	IF Group	87	79.29	**0.04** d=0.28
		non-IF Group	84	92.95	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	87	94.25	**0.02** d=0.34
		non-IF Group	84	77.46	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	IF Group	87	91.88	0.06
		non-IF Group	84	79.91	
Male	How fast do you	IF Group	6	14.50	0.78

	learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	non-IF Group	24	15.75	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	6	20.75	0.10
		non-IF Group	24	14.19	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	IF Group	6	13.00	0.46
		non-IF Group	24	16.13	
18-30 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	IF Group	26	27.27	0.29
		non-IF Group	32	31.31	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	26	32.33	0.21
		non-IF Group	32	27.20	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very	IF Group	26	34.77	**0.01** d=0.59
		non-IF Group	32	25.22	

	bad“)				
31-45 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	IF Group	37	33.84	0.09
		non-IF Group	37	41.16	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	37	41.42	0.09
		non-IF Group	37	33.58	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	IF Group	37	38.84	0.51
		non-IF Group	37	36.16	
46-65 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	IF Group	24	19.04	0.52
		non-IF Group	15	21.53	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	IF Group	24	21.02	0.48
		non-IF Group	15	18.37	
	How do you appreciate your health condition?	IF Group	24	19.31	0.64
		non-IF Group	15	21.10	

	(1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)				

*If the results are significant, the effect size of Cohen's d is also given for the U-test. The size of the effect size is interpreted as follows: Small effect: d=0.20 Average effect: d=0.50 Large effect: d=0.80.

Table 6 Results of the U-test for hypothesis 1 regarding cognitive abilities and health condition

To test the cognitive abilities of the participants, 3 exercises were inspired from an online resource for psychometric tests preparation called Prep Terminal. These exercises were pre-tested by a sample of 10 people selected prior to the publishing of the survey. The average solving time for each exercise was calculated and then used as a maximum time in the official survey for this study.

When analysing the cognitive abilities of the IF group and the non-IF group via crosstabs and chi quadrat test, there were significant group differences in the overall sample and in the female sample with regard to exercises 1 and 2. In exercise 1, the IF group gave a correct answer significantly more often than the non-IF group, while in exercise 2 they gave a wrong answer significantly more often than the non-If group.

The female sample of the young and the old age group also showed a significant group difference with regard to exercise 2. Here, too, the IF Group gave a wrong answer significantly more frequently.

The female sample of the young age group also showed a significant group difference with regard to exercise 3, with the IF group giving the wrong answer significantly more often.

The oldest female age group also showed a significant group difference with regard to exercise 1, with the IF group giving a correct answer significantly more often.

Total sample			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	57	81
		Expected Count	63.9	74.1
		% within IF Group	61.3%	75.0%

	Correct	Count	36	27
		Expected Count	29.1	33.9
		% within IF Group	38.7%	25.0%
	$X^2(1)= 4.37$, $p=0.04$, $\varphi^*=0.15$			
Total sample			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	70	64
		Expected Count	62.0	72.0
		% within IF Group	75.3%	59.3%
	Correct	Count	23	44
		Expected Count	31.0	36.0
		% within IF Group	24.7%	40.7%
	$X^2(1)= 5.76$, $p=0.02$, $\varphi^*=0.17$			
Total sample			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	38	38
		Expected Count	35.2	40.8
		% within IF Group	40,9%	35.2%
	Correct	Count	55	70
		Expected Count	57.8	67.2
		% within IF Group	59.1%	64.8%
	$X^2(1)=0.68$, $p=0.41$			
Female			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	54	66
		Expected Count	61.1	58.9
		% within IF Group	62.1%	78.6%

	Correct	Count	33	18
		Expected Count	25.9	25.1
		% within IF Group	37.9%	21.4%
	$X^2(1)=5.56$, $p=0.02$, $\varphi^*=0.18$			
Female			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	67	48
		Expected Count	58.5	56.5
		% within IF Group	77.0%	57.1%
	Correct	Count	20	36
		Expected Count	28.5	27.5
		% within IF Group	23.0%	42.9%
	$X^2(1)= 7.66$, $p=0.01$, $\varphi^*=0.21$			
Female			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	36	29
		Expected Count	33.1	31.9
		% within IF Group	41.4%	34.5%
	Correct	Count	51	55
		Expected Count	53.9	52.1
		% within IF Group	58.6%	65.5%
	$X^2(1)=0.85$, $p=0.36$			
Male			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	3	15
		Expected Count	3.6	14.4
		% within IF Group	50.0%	62.5%

	Correct	Count	3	9
		Expected Count	2.4	9.6
		% within IF Group	50.0%	37.5%
	$X^2(1)=0.31$, $p=0.58$			
Male			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	3	16
		Expected Count	3.8	15.2
		% within IF Group	50.0%	66.7%
	Correct	Count	3	8
		Expected Count	2.2	8.8
		% within IF Group	50.0%	33.3%
	$X^2(1)=0.57$, $p=0.45$			
Male			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	2	9
		Expected Count	2.2	8.8
		% within IF Group	33.3%	37.5%
	Correct	Count	4	15
		Expected Count	3.8	15.2
		% within IF Group	66.7%	62.5%
	$X^2(1)=0.04$, $p=0.85$			
18-30 years (female)			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	16	23
		Expected Count	17.5	21.5
		% within IF Group	61.5%	71.9%

	Correct	Count	10	9
		Expected Count	8.5	10.5
		% within IF Group	38.5%	28.1%
	$X^2(1)=0.70$, $p=0.40$			
18-30 years (female)			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	20	15
		Expected Count	15.7	19.3
		% within IF Group	76.9%	46.9%
	Correct	Count	6	17
		Expected Count	10.3	12.7
		% within IF Group	23.1%	53.1%
	$X^2(df)=5.41$, $p=0.02$, $\varphi^*=0.31$			
18-30 years (female)			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	14	9
		Expected Count	10.3	12.7
		% within IF Group	53.8%	28.1%
	Correct	Count	12	23
		Expected Count	15.7	19.3
		% within IF Group	46.2%	71.9%
	$X^2(1)=3.97$, $p=0.05$, $\varphi^*=0.26$			
31-45 years (female)			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	24	29
		Expected Count	26.5	26,5
		% within IF Group	64.9%	78.4%

	Correct	Count	13	8
		Expected Count	10.5	10.5
		% within IF Group	35.1%	21.6%
	$X^2(1)=1.66$, $p=0.20$			
31-45 years (female)			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	25	24
		Expected Count	24.5	24,5
		% within IF Group	67.6%	64.9%
	Correct	Count	12	13
		Expected Count	12.5	12.5
		% within IF Group	32.4%	35.1%
	$X^2(1)=0.06$, $p=0.81$			
31-45 years (female)			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	10	16
		Expected Count	13.0	13.0
		% within IF Group	27.0%	43.2%
	Correct	Count	27	21
		Expected Count	24.0	24.0
		% within IF Group	73.0%	56.8%
	$X^2(1)=2.14$, $p=0.14$			
46-65 years (female)			**IF Group**	**non-IF Group**
Exercise 1	Wrong	Count	14	14
		Expected Count	17.2	10.8
		% within IF Group	58.3%	93.3%

	Correct	Count	10	1
		Expected Count	6.8	4.2
		% within IF Group	41.7%	6.7%
	$X^2(1)=5.58$, $p=0.02$, $\varphi^*=0.38$			
46-65 years (female)			**IF Group**	**non-IF Group**
Exercise 2	Wrong	Count	22	9
		Expected Count	19.1	11.9
		% within IF Group	91.7%	60.0%
	Correct	Count	2	6
		Expected Count	4.9	3.1
		% within IF Group	8.3%	40.0%
	$X^2(1)=5.67$, $p=0.02$, $\varphi^*=0.38$			
46-65 years (female)			**IF Group**	**non-IF Group**
Exercise 3	Wrong	Count	12	4
		Expected Count	9.8	6.2
		% within IF Group	50.0%	26.7%
	Correct	Count	12	11
		Expected Count	14.2	8.8
		% within IF Group	50.0%	73.3%
	$X^2(1)=2.08$, $p=0.15$			

*For significant results with two nominally scaled variables, the phi coefficient (φ) is given. The effect size is interpreted as follows: small effect: φ=0.10; average effect: φ=0.30; large effect: φ=0.50.

Table 7 Results of the cross tabulation and the chi-square test for hypothesis 1 regarding cognitive abilities

Looking at a possible correlation between risk factors and intermittent fasting, the chi-square test showed no significant differences between the IF and the non-IF group as shown in the table below.

Total sample			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	28	39
		Expected Count	31.0	36.0
		% within IF Group	30.1%	36.1%
	No	Count	65	69
		Expected Count	62.0	72.0
		% within IF Group	69.9%	63.9%
	$X^2(1)=0.81$, $p=0.37$			
Female			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	28	30
		Expected Count	29.5	28.5
		% within IF Group	32.2%	35.7%
	No	Count	59	54
		Expected Count	57.5	55.5
		% within IF Group	67.8%	64.3%
	$X^2(1)=0.24$, $p=0.63$			
Male			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	0	9
		Expected Count	1.8	7.2
		% within IF Group	0.0%	37.5%
	No	Count	6	15

		Expected Count	4.2	16.8
		% within IF Group	100.0%	62.5%
	$X^2(1)=3.21$, $p=0.07$			
18-30 years (female)			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	6	5
		Expected Count	4.9	6.1
		% within IF Group	23.1%	15.6%
	No	Count	20	27
		Expected Count	21.1	25.9
		% within IF Group	76.9%	84.4%
	$X^2(1)=0.52$, $p=0.47$			
31-45 years (female)			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	9	15
		Expected Count	12.0	12.0
		% within IF Group	24.3%	40.5%
	No	Count	28	22
		Expected Count	25.0	25.0
		% within IF Group	75.7%	59.5%
	$X^2(1)=2.22$, $p=0.14$			
46-65 years (female)			**IF Group**	**non-IF Group**
Risk factors	Yes	Count	13	10
		Expected Count	14.2	8.8
		% within IF Group	54.2%	66.7%
	No	Count	11	5

		Expected Count	9.8	6.2
		% within IF Group	45.8%	33.3%
	$X^2(1)=0.60$, $p=0.44$			

Table 8 Results of the cross tabulation and the chi-square test for hypothesis 1 regarding risk factors.

To conclude, regarding the BMI and quality of life, IF did not show any significant impact on the participants of this study. When looking at the health status of the participants, a significant difference was found in the group of women aged between 18 – 30 years, where the ones practicing IF subjectively appreciated their health to be in a worse state than the group that didn't do IF. This result imposes the question if the subjects started to practice IF because they were in a bad health condition, hoping to improve. Taking cognitive abilities into consideration, there are differences between the two groups, meaning that significantly more subjects that practice IF stated that they learn new information faster compared to those that don't do IF. Also, when asked how forgetful they considered themselves to be, significantly less subjects of the IF-group declared to be forgetful compared to the ones that don't fast. These results regarding cognition were also apparent in the subgroup of female participants. Taking a look at the answers to the cognitive ability questions, the results are not homogenous. For exercise 1 the IF group answered the question significantly more often correctly than those who don't. This was also confirmed in the subgroup of females aged between 46 - 65 years. At the second exercise, it was the Non-IF group that answered the question significantly more often correctly than the IF group. This result was then also visible in the subgroup of females aged between 18 - 30 years and 46 - 65 years. The third exercise was answered correctly also significantly more often in the Non-IF group for females aged between 18 – 30 years. Furthermore, there were no significant differences apparent concerning the existence of risk factors and diseases between the subjects that practiced and those that didn't practice IF. Summing up, the first hypothesis could only be partially confirmed; meaning that IF appears to have a positive impact on forgetfulness and the ability to learn new information, but other than that no other impact on BMI, quality of life or risk factors and diseases could be concluded.

Results and discussion hypothesis 2

"Food intake outside of the circadian rhythm has a negative impact on body weight, metabolic and cardio-metabolic parameters (like glucose levels, insulin sensitivity, lipids and blood pressure), sleep quality, quality of life and cognitive abilities."

To test whether eating outside the circadian rhythm has a negative impact on health, two groups were created, “Group before 18 o'clock”, that ate their last meal before 6 pm. and “Group after 18 o'clock”, that ate their last meal at or after 6 pm. The table below shows the frequencies of both groups.

	Total sample		**Female**		**18-30 years (female)**		**31-45 years (female)**		**46-65 years (female)**	
	N	**%**	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**
Group before 18 o'clock	20	9.9	19	11.0	5	8.6	6	8.0	8	20.0
Group after 18 o'clock	182	89.7	153	88.4	53	91.4	69	92.0	31	77.5

Table 9 Frequencies for “Group before 18 o'clock” and “Group before 18 o'clock”. Mean age for the Group before 18 o’clock: 40.25 years (St. Dev.: 11.05); mean age for the “Group after 18 o'clock”: 36.68 years (St. Dev.: 10.59).

A t-test was used to investigate whether there is any significant difference between the two groups regarding BMI, quality of life and of sleep. There were no significant differences in the whole sample, nor where there in the female or male groups or in the different age groups for women.

Furthermore, a U-test was used to check whether there are any differences between groups regarding how fast they learn new information, forgetfulness and health condition. Here, there was noticed a significant difference in the female group aged 18 - 30 years belonging to the “Group before 18 o'clock” regarding their faster learning ability in contrast to those that eat later than 6 pm as shown below.

		Group	***N***	**Mean Rank**	***p*** ***d***
Total sample	How fast do you learn new	Group before 18 o'clock	20	90.75	0.32

	information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	Group after 18 o'clock	182	102.68	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Group before 18 o'clock	20	103.90	0.83
		Group after 18 o'clock	182	101.24	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Group before 18 o'clock	20	95.35	0.55
		Group after 18 o'clock	182	102.18	
Female	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	Group before 18 o'clock	19	77.18	0.33
		Group after 18 o'clock	153	87.66	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Group before 18 o'clock	19	88.92	0.81
		Group after 18 o'clock	153	86.20	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Group before 18 o'clock	19	80.37	0.49
		Group after 18 o'clock	153	87.26	
18-30 years (female)	How fast do you learn new information? (1-	Group before 18 o'clock	5	15.00	**0.04** d=0.25
		Group after	53	30.87	

	„very fast“, 2 – „average“, 3 – „difficult“)	18 o'clock			
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Group before 18 o'clock	5	30.70	0.87
		Group after 18 o'clock	53	29.39	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Group before 18 o'clock	5	26.50	0.69
		Group after 18 o'clock	53	29.78	
31-45 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	Group before 18 o'clock	6	33.00	0.50
		Group after 18 o'clock	69	38.43	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Group before 18 o'clock	6	45.17	0.37
		Group after 18 o'clock	69	37.38	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Group before 18 o'clock	6	29.75	0.23
		Group after 18 o'clock	69	38.72	
46-65 years (female)	How fast do you learn new information? (1- „very fast“, 2 –	Group before 18 o'clock	8	23.06	0.40
		Group after 18 o'clock	31	19.21	

	„average“, 3 – „difficult“)				
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Group before 18 o'clock	8	16.06	0.28
		Group after 18 o'clock	31	21.02	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Group before 18 o'clock	8	19.88	0.99
		Group after 18 o'clock	31	20.03	

Table 10 Results of the U-test for hypothesis 2 regarding ability to learn new information, forgetfulness and health condition.

A chi-quadrat test was performed to see if there are any differences between groups regarding ability to answer correctly to the cognitive questions and there were no significant results found. Also, there was no significant difference regarding risk factors between the two groups.

Furthermore, to test the second hypothesis two more groups were created, one of those who eat breakfast “Breakfast yes” and one of those that skip breakfast, “Breakfast no”. The frequencies of these two groups are shown below.

	Total sample		**Female**		**Male**		**18-30 years (female)**		**31-45 years (female)**		**46-65 years (female)**	
	N	**%**	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**	***N***	**%**
Breakfast yes	111	54.7	88	50.9	23	76.7	34	58.6	35	46.7	19	47.5
Breakfast no	92	45.3	85	49.1	7	23.3	24	41.4	40	53.3	21	52.5

Table 11 Frequencies for breakfast yes/no. Mean age for the "Breakfast yes" group: 36.02 years (St. Dev.: 10.23); mean age for the "Breakfast no" group: 38.39 years (St. Dev.:11.09).

A t-test was performed to see whether having or skipping breakfast has a significant influence on BMI, quality of life and of sleep and the results showed no significant differences between groups.

		Breakfast	***N***	**Mean Rank**	***p***
Total sample	How fast do you learn new information? (1- „very fast", 2 – „average", 3 – „difficult")	Yes	111	107.13	0.12
		No	92	95.82	
	Are you often forgetful? (1- „yes", 2 - „sometimes", 3 - „no")	Yes	111	95.83	0.08
		No	92	109.45	
	How do you appreciate your health condition? (1 – „very good", 2 – „good", 3 – „bad", 4 – „very bad")	Yes	111	96.15	0.06
		No	92	109.06	
Female	How fast do you learn new information? (1- „very fast", 2 – „average", 3 – „difficult")	Yes	88	92.19	0.12
		No	85	81.63	
	Are you often	Yes	88	80.80	0.07

	forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	No	85	93.42	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Yes	88	79.88	**0.02** d=0.29
		No	85	94.38	
Male	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	Yes	23	14.93	0.53
		No	7	17.36	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Yes	23	15.22	0.77
		No	7	16.43	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Yes	23	16.07	0.53
		No	7	13.64	
18-30 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 –	Yes	34	31.21	0.29
		No	24	27.08	

	„difficult“)				
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Yes	34	27.43	0.23
		No	24	32.44	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Yes	34	25.13	**0.01** d=0.65
		No	24	35.69	
31-45 years (female)	How fast do you learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	Yes	35	38.29	0.90
		No	40	37.75	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Yes	35	38.09	0.97
		No	40	37.93	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Yes	35	33.64	**0.05** d=0.38
		No	40	41.81	
46-65 years	How fast do you	Yes	19	23.82	0.09

(female)	learn new information? (1- „very fast“, 2 – „average“, 3 – „difficult“)	No	21	17.50	
	Are you often forgetful? (1- „yes“, 2 - „sometimes“, 3 - „no“)	Yes	19	16.66	**0.05** d=0.66
		No	21	23.98	
	How do you appreciate your health condition? (1 – „very good“, 2 – „good“, 3 – „bad“, 4 – „very bad“)	Yes	19	23.13	0.18
		No	21	18.12	

Table 12: Results of U-Test for hypothesis 2 (breakfast)

On the other hand, when performing a U-test for the ability to learn new information, forgetfulness and health condition between the two groups, there were significant differences. Looking at the overall sample, there can be no significant impact noticed regarding health condition, but among females, the ones having breakfast believe to have a significant better health than the ones that don’t. This effect can be found again in two of the three age categories in the female sample (18 – 30 years and 31 – 45 years of age). Another significant effect becomes apparent regarding cognitive abilities, specifically forgetfulness, in the female sample aged 41 – 65 years. Here, surprisingly, the ones that don’t eat breakfast declare to be less forgetful than the ones that do. Next, we will analyse if there are any significant differences between the two groups when solving the cognitive ability exercises. Looking at the overall sample, the group that has breakfast solved exercise 2 significantly more often correctly than that which doesn’t. The same effect can be seen then in the overall group of females and in the group of females aged 18 – 30 years.

Total sample			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	79	61
		Expected Count	76.6	63.4
		% within IF Group	71.2%	66.3%
	Correct	Count	32	31
		Expected Count	34.4	28.6
		% within IF Group	28.8%	33.7%
	$X^2(1)=0.56$, $p=0.46$			
Total sample			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	67	69
		Expected Count	74.4	61.6
		% within IF Group	60.4%	75.0%
	Correct	Count	44	23
		Expected Count	36.6	30.4
		% within IF Group	39.6%	25.0%
	$X^2(1)=4.88$, $p=0.03$, $\varphi=0.16$			
Total sample			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	39	37
		Expected Count	41.6	34.4
		% within IF Group	35.1%	40.2%
	Correct	Count	72	55
		Expected Count	69.4	57.6
		% within IF Group	64.9%	59.8%
	$X^2(1)=0.56$, $p=0.46$			
Female			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	66	56
		Expected Count	62.1	59.9
		% within IF Group	75.0%	65.9%
	Correct	Count	22	29
		Expected Count	25.9	25.1
		% within IF Group		
	$X^2(1)=1.73$, $p=0.19$			
Female			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	52	65
		Expected Count	59.5	57.5
		% within IF Group	59.1%	76.5%

	Correct	Count	36	20
		Expected Count	28.5	27.5
		% within IF Group	40.9%	23.5%
	$X^2(1)=5.97$, $p=0.02$, $\varphi=0.19$			
Female			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	30	35
		Expected Count	33.1	31.9
		% within IF Group	34.1%	41.2%
	Correct	Count	58	50
		Expected Count	54.9	53.1
		% within IF Group	65.9%	58.8%
	$X^2(1)=0.96$, $p=0.34$			
Male			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	13	5
		Expected Count	13.8	4.2
		% within IF Group	56.5%	71.4%
	Correct	Count	10	2
		Expected Count	9.2	2.8
		% within IF Group	43.5%	28.6%
	$X^2(1)=0.5$, $p=0.48$			
Male			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	15	4
		Expected Count	14.6	4.4
		% within IF Group	65.2%	57.1%
	Correct	Count	8	3
		Expected Count	8.4	2.6
		% within IF Group	34.8%	42.9%
	$X^2(1)=0.15$, $p=0.70$			
Male			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	9	2
		Expected Count	8.4	2.6
		% within IF Group	39.1%	28.6%
	Correct	Count	14	5
		Expected Count	14.6	4.4
		% within IF Group	60.9%	71.4%
	$X^2(1)=0.26$, $p=0.61$			

18-30 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	24	15
		Expected Count	22.9	16.1
		% within IF Group	70.6%	62.5%
	Correct	Count	10	9
		Expected Count	11.1	7.9
		% within IF Group	29.4%	37.5%
	$X^2(1)=0.42$, $p=0.52$			
18-30 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	18	17
		Expected Count	20.5	14.5
		% within IF Group	52.9%	70.8%
	Correct	Count	16	7
		Expected Count	13.5	9.5
		% within IF Group	47.1%	29.2%
	$X^2(df)=1.88$, $p=0.17$			
18-30 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	9	14
		Expected Count	13.5	9.5
		% within IF Group	26.5%	58.3%
	Correct	Count	25	10
		Expected Count	20.5	14.5
		% within IF Group	73.5%	41.7%
	$X^2(1)=5.97$, $p=0.02$, $\varphi=0.19$			
31-45 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	26	28
		Expected Count	25.2	28.8
		% within IF Group	74.3%	70.0%
	Correct	Count	9	12
		Expected Count	9.8	11.2
		% within IF Group	25.7%	30.0%
	$X^2(1)=0.170$, $p=0.68$			
31-45 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	21	29
		Expected Count	23.3	26.7
		% within IF Group	60.0%	72.5%

	Correct	Count	14	11
		Expected Count	11.7	13.3
		% within IF Group	40.0%	27.5%
	$X^2(1)=1.31$, $p=0.25$			
31-45 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	16	10
		Expected Count	12.1	13.9
		% within IF Group	45.7%	25.0%
	Correct	Count	19	30
		Expected Count	22.9	26.1
		% within IF Group	54.3%	75.0%
	$X^2(1)=3.57$, $p=0.06$			
46-65 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 1	Wrong	Count	16	13
		Expected Count	13.8	15.2
		% within IF Group	84.2%	61.9%
	Correct	Count	3	8
		Expected Count	5.2	5.8
		% within IF Group	15.8%	38.1%
	$X^2(1)=2.49$, $p=0.12$			
46-65 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 2	Wrong	Count	13	19
		Expected Count	15.2	16.8
		% within IF Group	68.4%	90.5%
	Correct	Count	6	2
		Expected Count	3.8	4.2
		% within IF Group	31.6%	9.5%
	$X^2(1)=3.03$, $p=0.08$			
46-65 years (female)			**Breakfast yes**	**Breakfast no**
Exercise 3	Wrong	Count	5	11
		Expected Count	7.6	8.4
		% within IF Group	26.3%	52.4%
	Correct	Count	14	10
		Expected Count	11.4	12.6
		% within IF Group	73.7%	47.6%
	$X^2(1)=2.82$, $p=0.09$			

Table 13 Cross tabulation and Chi-Square Test Results for Hypothesis 2 (breakfast).

When analysing the risk factors, having breakfast doesn't seem to have any significant impact on them.

Furthermore, the question arose if night shifts impact the quality of life. For that, a t-test for independent samples was used that showed no significant differences. A Pearson's Correlation was also calculated for the number of night shifts and the quality of life, also returning no significant results.

Also, night shifts and cognitive abilities were analysed. There was no significant impact of having night shifts on the self-evaluation of forgetfulness and the ability to learn new information or on the ability to answer correctly to the cognitive exercises.

Age also didn't have any significant impact on the ability to answer correctly to the cognitive tasks.

Then we categorized the sample of subjects into three categories of occupation, studying, employed and unemployed. In total there were 193 subjects that could be attributed to one of the three categories. The aim was to test whether occupation links to cognitive abilities like forgetfulness, ability to learn new information and ability to answer correctly to the cognitive questions. None yielded in any significant difference between groups.

To sum up, analysing the results of the second hypothesis, regarding BMI, quality of life, quality of sleep and risk factors and diseases, there are no significant differences between those that have food intake within or those that have it outside of the circadian rhythm. On the other hand, when taking cognitive abilities into account, results show that significantly more of those that have their last meal before 6 pm and so according to the circadian rhythm, learn new information more quickly than those who eat outside the circadian rhythm. Also, the answers to the cognitive ability exercises were this time homogenous, showing that those who consume breakfast have answered exercise 2 significantly more often correctly than those who don't have breakfast. This result was then also apparent in the subgroup of females. Furthermore, exercise 3 was also answered significantly more often correctly by females aged between 18-30 years that have breakfast in comparison to those that don't. On the other hand, the category of women aged 46 - 60 years that skip breakfast consider themselves to be less forgetful. Regarding health status, significantly more females that eat breakfast estimate their health condition to be better than those who skip breakfast. This result was then also visible in the subgroups of females aged between 18 - 30 years and 31 – 45 years. To conclude, the second hypothesis was only partially confirmed, results show that food intake outside the circadian rhythm has a negative impact on cognitive abilities, specifically on the ability to perform cognitive ability exercises and

ability to learn new information and on the health status, while no impact on BMI, quality of life and of sleep, risk factors and diseases could be established.

4.5. Limitations and further research suggestions

Limitations of this study are represented by the fact that the survey was conducted online. This led to not being able to guide the subjects through the questions of the survey and give possible explanations when necessary. Also, being online, the hour at which the survey was conducted was not within a time frame for all participants, but random. This could have influenced the answers to the cognitive ability exercises, as it could make a difference solving a cognitive problem with a clear head or solving it after a long, tiring day. Furthermore, it could be that subjects complete the questionnaire in a rush and don't take their time to reflect on the answers when doing it online, whereas doing it in person could encourage them to give more authentic answers. Another limitation of this study is the fact that it was women that mostly completed the survey, whereas men had a much lower availability in doing so. Another question that could be very helpful in the analysing of the data would be for how long the subject has been practicing IF or has been eating according to the circadian rhythm. Taking all this into consideration, further research on this topic could yield very promising results.

5. CONCLUSIONS

Animal studies on fasting show significant positive influences on many health related aspects, like their life-span, body weight and composition, metabolic parameters, like glucose and insulin levels, leptin and adiponectin. Also, inflammation and cardiovascular parameters appear to be impacted in a positive manner by fasting. Their cognitive abilities and motoric coordination are two further aspects that show improvement under a fasting regime. [9, 3, 12, 13, 14, 15, 21, 25, 26, 36]

These results could partially be replicated also in human clinical trials. Literature research shows that fasting positively impacts body weight and body composition. Furthermore, fasting has a positive influence on metabolic parameters like LDL, TG, IGF-1, C-Reactive Protein and insulin. Also, fasting appears to have a positive effect on cardio-metabolic parameters like blood pressure. The impact of fasting on some metabolic and cardio-metabolic parameters seems to be even greater when it is associated with the circadian rhythm, which implies that food intake is most beneficial when it is happening in the morning and at midday and decreases towards the evening. [45, 46, 47, 48, 54, 58, 50, 59, 60 - 64]

The present master thesis aimed to resume the existing evidence regarding the consequences of fasting and of food intake within and without the circadian rhythm for animals, as well as for humans and to assess whether these impacts can be confirmed in large variety of human subjects with ages between 18 and 65 years, both female and male, healthy or suffering from diseases outside of clinical trials, living day by day life.

After gathering data from 203 subjects via an online survey and analysing it statistically, it could be confirmed that fasting has a positive influence on cognitive abilities, like learning new information and forgetfulness. Furthermore, it could be proven that food intake according to the circadian rhythm is also positively linked to cognitive abilities like learning new information or solving cognitive ability exercises. Also, the health condition of the subjects that adhered to the circadian rhythm was significantly better than of those who didn’t.

Other parameters included in the hypotheses, like BMI, quality of life, quality of sleep and risk factors and diseases could not be confirmed within this study but taking into account the limitations of this study, like it being an online survey with no means to answer possibly arising questions, the different completion time of the survey for each participant, the small percentage of men taking part in this study and the lack of two important questions about motive for doing IF and duration since starting to fast could all have played a part in these final results.

6. SUMMARY

6.1 BACKGROUND

Fasting has become an increasingly popular practice in the last years and there is a lot of research regarding its benefits on the health of humans. Early animal studies have shown its positive impact on life-span, bodyweight and body composition, metabolic and cardio-metabolic parameters, as well as on cognitive functions. Human studies have succeeded in replicating these results. As cardiovascular diseases, diabetes and cognitive disorders are some of the most important public health concerns worldwide and obesity and dislipedemia presenting major risk factors, research for prevention and therapy methods for these risk factors and diseases present a major interest. Given the positive impacts of fasting in clinical trials, this study aims to investigate whether fasting and a life-style in accordance to the circadian clock can confirm these results when a random and varied range of individuals living day by day life is assessed.

6.2 METHODS

In order to assess this, a survey consisting of 47 questions was distributed online and answered by 203 female and male subjects aged between 18 – 60 years old. To distribute the survey, social media platforms were used. Since the survey was bilingual, it was distributed to German speaking groups, as well as to English speaking ones.

6.3 RESULTS

Out of the total of 203 participants, 173 were women and 30 men. The subject's mean age was 37.09 (Std. Dev. ± 10.67) years and their mean BMI 26.42 (Std. Dev. ± 8.18). 40.46% of the women and 33.33% of the men don't exercise regularly, while 39.88% of women and 30% of men exercise at least 1 - 3 hours per week. About 66.7% of the subjects consider their health to be in good condition, while 23.3% define it as very good. Regarding the annual health control, only 44% of the female subjects and 53.3% of men declare to consider it. A percentage of 54.7% of all participants use a step counter and on average women walk about 8642 steps and men 8424 steps. Risk factors like elevated blood sugar, blood lipids or blood pressure or chronic diseases are found in 33.5% of women and 30% of men. The most common of them is high blood pressure, with a percentage of 11.3%, followed by high blood lipids with a percentage of 8.9% and high fasting glucose or high HbA1c with a percentage of 6.4%. Diabetes type II is found in 4.4% of the subjects and heart attacks and stroke is represented only in 0.5% of the subjects. Other risk factors and diseases are found in 14.3% of the participants. Regarding nutrition, 54.7% of the subjects have a mixed type of diet, 22.66% declare to practice IF, vegetarians are represented by 8.37% of the subjects, pescetarians are found with a percentage of 5.42%, adapts of the ketogenic diet are 4.93% and vegans and adapts of raw or paleo diet are represented by less than 5%. 73.73% of the subjects have regular sleeping times and 13.9 % have night

shifts at least once a month. IF appears to have no impact on the BMI, quality of life or risk factors and diseases of the subjects. On the other hand, IF showed a significant influence on cognitive abilities like forgetfulness and the ability to learn new information. Furthermore, analysing the impact of food intake according to the circadian clock, this appears to have a significant positive impact also on cognitive abilities like the capacity of learning new information and the ability to solve cognitive ability exercises. Another parameter positively influenced by the food intake according to the circadian rhythm is the personal health estimation of the subjects, while BMI, quality of life and sleep and risk factors and diseases seem to have not been impacted by this.

6.4 CONCLUSION

Results show parameters like cognitive abilities and health status to be significantly influenced by fasting and the circadian rhythm.

7. ZUSAMMENFASSUNG

7.1 HINTERGRUND

Fasten ist in den letzten Jahren zu einer immer beliebteren Praxis geworden, und es gibt viele Untersuchungen zu den Vorteilen für die Gesundheit des Menschen. Frühe Tierstudien haben eine positive Auswirkung von Fasten auf die Lebensdauer, das Körpergewicht und die Körperzusammensetzung, metabolische und kardiometabolische Parameter sowie auf die kognitiven Funktionen gezeigt. Humanstudien konnten diese Ergebnisse erfolgreich replizieren. Da Herz-Kreislauf-Erkrankungen, Diabetes und kognitive Störungen zu den wichtigsten Problemen der Gesundheitspolitik weltweit gehören und Adipositas und Dyslipidämie wichtige Risikofaktoren darstellen, ist die Erforschung von Präventions- und Therapiemethoden für diese Risikofaktoren und Krankheiten von großem Interesse. Angesichts der positiven Auswirkungen des Fastens in klinischen Studien soll die vorliegende Masterarbeit untersuchen, ob Fasten und ein Lebensstil gemäß der zirkadianen Uhr diese Ergebnisse bestätigen können, wenn eine zufällige Auswahl von Personen befragt werden.

7.2 METHODEN

Um dies zu beurteilen, wurde eine Umfrage bestehend aus 47 Fragen online verteilt und von 203 weiblichen und männlichen Probanden im Alter zwischen 18 – 60 Jahren beantwortet. Zur Verbreitung der Umfrage wurden Social-Media-Plattformen genutzt. Da die Umfrage zweisprachig war, wurde sie sowohl in deutschsprachigen als auch in englischsprachigen Gruppen verteilt.

7.3 ERGEBNISSE

Von den insgesamt 203 Teilnehmern waren 173 Frauen und 30 Männer. Das mittlere Alter der Probanden betrug 37,09 Jahre (Std.-Abw. ± 10,67) und ihr mittlerer BMI 26,42 (Std.-Abw. ± 8,18). 40,46 % der Frauen und 33,33 % der Männer bewegen sich nicht regelmäßig, während 39,88 % der Frauen und 30 % der Männer mindestens 1 - 3 Stunden pro Woche Sport treiben. Rund 66,7 % der Probanden schätzen ihren Gesundheitszustand als gut ein, 23,3 % definieren ihn als sehr gut. Zur jährlichen Gesundheitskontrolle erklären sich nur 44 % der weiblichen Probanden und 53,3 % der Männer dazu bereit. 54,7 % aller Teilnehmer nutzen einen Schrittzähler und im Durchschnitt gehen Frauen etwa 8642 Schritte und Männer 8424 Schritte. Risikofaktoren wie erhöhte Blutzucker-, Blutfett- oder Blutdruckwerte oder chronische Erkrankungen finden sich bei 33,5 % der Frauen und 30 % der Männer. Der häufigste von ihnen ist Bluthochdruck mit einem Prozentsatz von 11,3 %, der zweithäufigste sind hohe Blutfette mit einem Prozentsatz von 8,9 % und der dritte ist gekennzeichnet durch einen hohen Nüchternblutzucker oder einen hohen HbA1c mit einem Prozentsatz von 6,4 %. Diabetes Typ II findet sich bei 4,4 % der Probanden und Herzinfarkt und Schlaganfall sind nur bei 0,5 % der Probanden vertreten. Andere Risikofaktoren und Erkrankungen finden sich bei 14,3 % der

Teilnehmer. In Bezug auf die Ernährung haben 54,7 % der Probanden eine gemischte Ernährungsweise, 22,66 % geben an, IF zu praktizieren, Vegetarier sind mit 8,37 % der Probanden vertreten, Pescetarier sind mit einem Prozentsatz von 5,42 % zu finden, Anhänger der ketogenen Ernährung sind mit 4,93 % und Veganer und Anhänger der Rohkost- oder Paleo-Ernährung sind mit weniger als 5 % vertreten. 73,73 % der Probanden haben regelmäßige Schlafenszeiten und 13,9 % haben mindestens einmal im Monat Nachtschichten. IF scheint keinen Einfluss auf den BMI, die Lebensqualität oder Risikofaktoren und Erkrankungen der Probanden zu haben. Andererseits zeigte die IF-Gruppe einen signifikanten Einfluss auf kognitive Fähigkeiten wie Vergesslichkeit und die Fähigkeit, neue Informationen zu lernen. Darüber hinaus scheint die Analyse der Auswirkungen der Nahrungsaufnahme gemäß der zirkadianen Uhr auch einen signifikanten positiven Einfluss auf die kognitiven Fähigkeiten zu haben, wie die Fähigkeit, neue Informationen zu lernen und die Fähigkeit, kognitive Übungen zu lösen. Ein weiterer Parameter, der durch die Nahrungsaufnahme gemäß dem zirkadianen Rhythmus positiv beeinflusst wird, ist der selbst bewertete Gesundheitszustand der Probanden, während BMI, Lebensqualität und Schlafqualität sowie Risikofaktoren und Krankheiten davon nicht beeinflusst zu sein scheinen.

7.4 SCHLUSSFOLGERUNG

Die Ergebnisse zeigen, dass Parameter wie kognitive Fähigkeiten und der selbst bewertete Gesundheitszustand durch Fasten und den zirkadianen Rhythmus signifikant positiv beeinflusst werden kann.

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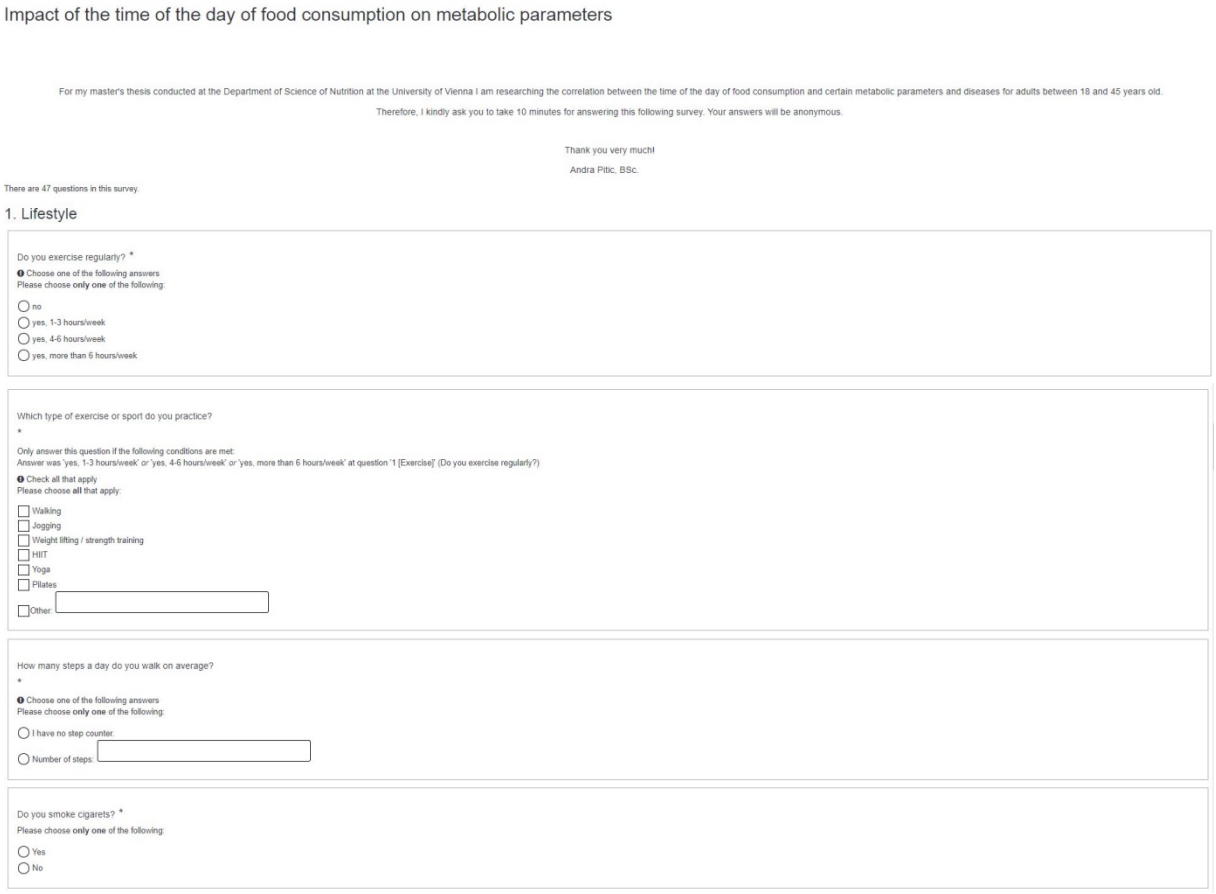
ANEXES

Survey



Impact of the time of the day of food consumption on metabolic parameters

For my master's thesis conducted at the Department of Science of Nutrition at the University of Vienna I am researching the correlation between the time of the day of food consumption and certain metabolic parameters and diseases for adults between 18 and 45 years old.
Therefore, I kindly ask you to take 10 minutes for answering this following survey. Your answers will be anonymous.

Thank you very much!
Andra Pitic, BSc.

There are 47 questions in this survey.

1. Lifestyle

Do you exercise regularly? *
Choose one of the following answers
Please choose only one of the following:
no
yes, 1-3 hours/week
yes, 4-6 hours/week
yes, more than 6 hours/week

Which type of exercise or sport do you practice?
*
Only answer this question if the following conditions are met:
Answer was 'yes, 1-3 hours/week' or 'yes, 4-6 hours/week' or 'yes, more than 6 hours/week' at question '1 [Exercise]' (Do you exercise regularly?)
Check all that apply
Please choose all that apply:
Walking
Jogging
Weight lifting / strength training
HIIT
Yoga
Pilates
Other:

How many steps a day do you walk on average?
*
Choose one of the following answers
Please choose only one of the following:
I have no step counter.
Number of steps:

Do you smoke cigarets? *
Please choose only one of the following:
Yes
No

Did you smoke cigarets in the past? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Do you drink alcohol? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

How much alcohol do you drink? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '6 [Alcohol]' (Do you drink alcohol?)

ℹ Choose one of the following answers
Please choose **only one** of the following:

- ◯ less than 1 glass (=1/8l) wine OR 1 beer (=0,3l) a day
- ◯ 1 glass of wine (=1/8l) OR 1 beer (=0,3l) a day (every day)
- ◯ more than 1 glass of wine (=1/8l) OR 1 beer (=0,3l) a day

How do you appreciate your quality of life?
*

Please choose the appropriate response for each item:

	1	2	3	4	5	6	7	8	9	10
1 is „very good" and 10 is „very poor"	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

2. Health

How do you appreciate your health condition?
*

ℹ Choose one of the following answers
Please choose **only one** of the following:

- ◯ very good
- ◯ good
- ◯ bad
- ◯ very bad

Do you do an annual health check? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Where there any risk factors (high blood pressure, high blood lipids, high blood sugar level, etc.) detected or any chronical diseases? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Which risk factors or chronical diseases were detected? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '11 [Riskfactors]' (Where there any risk factors (high blood pressure, high blood lipids, high blood sugar level, etc.) detected or any chronical diseases?)

ℹ Comment only when you choose an answer.
Please choose all that apply and provide a comment:

- ☐ High blood pressure (mmHg)
- ☐ High blood lipids (LDL in mg/dl or mmol/l; TG in mg/dl or mmol/l)
- ☐ High fasting glucose (mg/dl)
- ☐ High HbA1c (mg/dl)
- ☐ Diabetes Type II
- ☐ Heart attack
- ☐ Stroke
- ☐ Other:

Are you currently taking any medication? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Which medication are you currently taking? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '13 [Medication]' (Are you currently taking any medication?)

Please write your answer here:

3. Sleep

Do you have regular sleeping times? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

What time do you go to sleep? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '15 [Sleepingtimes]' (Do you have regular sleeping times?)

Please write your answer here:

What time do you wake up? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '15 [Sleepingtimes]' (Do you have regular sleeping times?)

Please write your answer here:

Do you sometimes have night shifts? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

How often in a month? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '18 [Nightshifts]' (Do you sometimes have night shifts?)

Please write your answer here:

How well rested do you wake up? *

Please choose the appropriate response for each item:

	1	2	3	4	5	6	7	8	9	10
1 is „very well rested" and 10 is „very tired"	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

4. Cognition

How fast do you learn new information? *

ℹ Choose one of the following answers
Please choose **only one** of the following:

- ◯ Very fast
- ◯ Average
- ◯ Very difficult

Are you often forgetful? *

ℹ Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No
- ◯ Sometimes

420 people are in a room. 172 understand English and 122 understand German. What percentage of the people don't understand neither English nor German?

*

Please write your answer here:

Suppose that all children in a classroom receive sweets. A lot of the colorful packed sweets also contain a surprise. Kathy didn't receive any surprise when she opened her sweet. Conclusion: Kathy has received a colorful packed sweet that didn't contain any surprise.

a) True b) False c) Cannot be determined with the provided information.

*

Please write your answer here:

9 cats in a shelter have the same numbers of toys. The dogs have 153 toys. Dogs and cats have together 234 toys. How many toys does each cat have?

*

Please write your answer here:

5. Nutrition

Do you have a particular type of nutrition? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

What type of nutrition do you have? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '26 [Ernweise]' (Do you have a particular type of nutrition?)

ℹ Comment only when you choose an answer.
Please choose all that apply and provide a comment:

- ☐ vegetarian (no meat & fish, but milk products and/or eggs)
- ☐ pescetarian (no meat, but fish and/or milk products and/or eggs)
- ☐ vegan (no animal products)
- ☐ ketogenic (low carb)
- ☐ Paleo (stone age nutrition)
- ☐ Raw
- ☐ Intermittent fasting Please fill in how many hours a day you fast and/or how many days in a week you fast (total food abstinence).

Other:

What time do you eat your last meal in a day?
*

Please write your answer here:

What time do you eat your main meal?
*

Please write your answer here:

During the week:

Do you have breakfast?
*

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

During the week:

What time do you have breakfast?
*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '31 [WeekBreakfast]' (During the week: Do you have breakfast?)

Please write your answer here:

During the week:

Do you have lunch?
*

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

During the week:

What time do you eat lunch?
*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '33 [WeekMM]' (During the week: Do you have lunch?)

Please write your answer here:

During the week:

Do you eat dinner?
*

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

During the week:

What time do you have dinner?

*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '35 [WeekDinner]' (During the week: Do you eat dinner?)

Please write your answer here:

On the weekends:

Do you have breakfast?

*

Please choose **only one** of the following:

◯ Yes
◯ No

On the weekends:

What time do you have breakfast?

*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '37 [WEBreakfast]' (On the weekends: Do you have breakfast?)

Please write your answer here:

On the weekends:

Do you have lunch?

*

Please choose **only one** of the following:

◯ Yes
◯ No

On the weekends:

What time do you have lunch?

*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '39 [MMWE]' (On the weekends: Do you have lunch?)

Please write your answer here:

On the weekends:

Do you have dinner?

*

Please choose **only one** of the following:

◯ Yes
◯ No

On the weekends:

What time do you have dinner?

*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '41 [WEDinner]' (On the weekends: Do you have dinner?)

Please write your answer here:

6. General information

Gender *

Please choose **only one** of the following:

◯ Female
◯ Male

Age *

ⓘ Only numbers may be entered in this field.
Please write your answer here:

Height (cm) *

ⓘ Only numbers may be entered in this field.
Please write your answer here:

Weight (kg) *

ⓘ Only numbers may be entered in this field.
Please write your answer here:

Occupation

Please write your answer here:

Thank you for taking part in this survey!