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HOW SLEEP RESTRICTION, OR INADEQUATE SLEEP, MAY AFFECT INDIVIDUAL NON-ESTERIFIED FATTY ACID CONCENTRATIONS IN THE HUMAN BODY

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ABSTRACT

Sleep is essential for human health and it plays a critical role in maintaining physical health, such as supporting cardiovascular health, metabolism, and weight management. Unfortunately, inadequate sleep is prevalent in the United States. According to the Centers for Disease Control and Prevention (CDC), one in three adults in the U.S. does not get enough sleep. Inadequate sleep has been linked to several health problems, such as diabetes, obesity, and depression. High-fat meals are also a concern in the U.S. diet. A high-fat diet can contribute to the development of chronic diseases such as heart disease, type 2 diabetes, and obesity. According to a report from the National Center for Health Statistics, about one-third of adults in the United States consume fast food on any given day, and fast food tends to be high in fat and calories. Previous work has assessed the total non-esterified fatty acid (NEFA) concentration of 5 h time in bed (TIB) per night for four consecutive nights for sleep restriction following a standardized high-fat dinner (HFD) followed by one night of recovery sleep (10 h TIB). Results showed that sleep restriction decreased total NEFA throughout the high-fat meal and NEFA remained suppressed in the recovery condition.

In this study, we used the samples from the NEFA parent study. We examined how individual NEFA responds to a standardized high-fat dinner in young healthy men under sleep restriction and after recovery. Compared with the baseline value, the saturated fatty acids (myristic acid: $p=0.81$, palmitic acid: $p=0.81$, stearic acid: $p=0.56$) were not significantly suppressed but the unsaturated fatty acids (oleic acid: $p=0.087$, linoleic acid: $p=0.069$) were significantly suppressed during sleep restriction. After allowed recovery, the five fatty acids (myristic acid: $p=0.99$, palmitic acid: $p=0.58$, stearic acid: $p=0.58$, oleic acid: $p=0.24$, linoleic acid: $p=0.12$) were not significantly different from the baseline. In conclusion, we found sleep

restriction inhibited normal suppression of unsaturated, but not saturated, fatty acids in response to a HFD which was restored after allowed sleep recovery.

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Chapter 1 Introduction

Non-esterified Fatty Acid

Non-esterified fatty acids (NEFA) are free fatty acids that contribute only a small proportion of the body's fat but are still an important metabolic fuel in the human body. NEFA consist of long-chain fatty acids, medium-chain fatty acids, and short-chain fatty acids[1]. Fatty acids can be esterified into triacylglycerol (TG) and stored in adipose tissue and transported to other tissues for energy use. NEFA can also circulate in the bloodstream, bound to the protein albumin, and is produced when TG is broken down and released from adipose tissue into the bloodstream. During periods of fasting, nearly all NEFA in the bloodstream originates from adipose tissue. However, following a meal that contains fat, a process called spillover occurs where enzymes in adipose tissue break down TG in the bloodstream, releasing NEFA into circulation[2]. Research has shown NEFA is important for the induction of insulin resistance in the human body. Modulation of hormonal signaling which is affected by diet led to an increase in NEFA mobilization in the post-absorptive state, whereas NEFA mobilization was inhibited in the postprandial state[3]. The concentration of NEFA varies widely from hour to hour through the blood circulation, reflecting nutritional state and physical activity[4]. Inappropriately increased concentration of plasma NEFA may have some adverse effects on both carbohydrate and lipid metabolism and these effects are likely to be most marked in the postprandial period when NEFA release from adipose tissue is usually suppressed[4]. Previous research has shown, in

healthy young men fed a standardized high-fat diet, postprandial (TG) was suppressed during sleep restriction but it was recovered to baseline value after one night of recovery sleep. However, during the standardized high-fat diet, NEFA was suppressed during sleep restriction and remained suppressed after one night of recovery sleep[5]. The release of insulin quickly suppresses the mobilization of fat, causing the concentration of NEFA in the blood to decrease after consuming a meal containing carbohydrates, which increases insulin level in the blood. Although excess fatty acids can mitigate this impact, they do not completely counteract it.

The Randle cycle, also called the glucose fatty-acid cycle, is a metabolic process that the competition between glucose and fatty acids as fuel selection for muscle and adipose tissue. Insulin which is a hormone that is secreted while blood glucose is high restricts lipolysis and promotes lipogenesis to reduce NEFA concentration. In the postprandial period, the insulin level is high so the adipose tissue prefers to use glucose as fuel. In the pre-prandial period, the insulin level is low so the adipose tissue prefers to use fatty acid as fuel[6]. As a result, the daily pattern of NEFA levels in the blood exhibits the highest levels after an extended period without eating, followed by a decrease after each meal[2]. In addition, research indicates that individuals with upper-body/visceral obesity exhibit increased rates of adipose tissue lipolysis, leading to higher concentrations of NEFA[7]. In general, men have a greater amount of visceral fat compared to women. Men not only have larger fat cells, but also a greater number of visceral fat cells than women[8]. Although there are regional differences in the production of leptin and cytokines by adipose tissue, the most significant and consistent abnormality of lipolysis in visceral obesity is abnormal suppression of NEFA release during the postprandial period, resulting from an attenuated suppression of lipolysis by insulin. Visceral fat area correlates positively with NEFA release during hyperinsulinaemia, confirming the association between visceral fat and

dysregulation of lipolysis. However, the research shows that increased visceral fat is not the predominant source of NEFA release. The study found that regional differences in adipose tissue uptake of fatty acids may be an essential determinant of body fat distribution, which in turn appears to predict abnormalities of fatty acid metabolism[7].

For the purpose of this study, we are going to focus on these five individual fatty acids: myristic acid (MA, C14:0), palmitic acid (PA, C16:0), stearic acid (SA, C18:0), oleic acid (OA, C18:1n9), and linoleic acid (LA, C18:2n6).

Myristic Acid

Myristic acid is present in low concentrations in human and animal tissues, making up only about 1% of the total endogenous fatty acids. Despite its minor presence, it has gained attention due to its potential association with metabolic disorders and cardiovascular disease (CVD)[9]. MA has been identified in the serum and liver of individuals with non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH)[10–12]. It also has a role in the modification of proteins through myristoylation, which can affect various signaling pathways and alter cellular functions[13,14]. Observations have linked high levels of MA in serum triglycerides with obesity and metabolic problems, while diet and exercise have been shown to reduce MA levels in people with metabolic syndrome[18]. While a connection between MA and CVD has been established, the effect of MA on systemic metabolism and its impact on obesity-related insulin resistance is still not well understood[9,15,16].

Palmitic Acid

Palmitic acid is the most common type of saturated fatty acid (20–30% of total fatty acids) that is present in the human body and can be obtained from the diet or produced internally through a process called de novo lipogenesis (DNL). PA is found in high amounts in palm oil, meat and dairy products, cocoa butter, and olive oil[17]. The risk of cardiovascular disease has been associated with western-style diets, specifically rich in SFA palmitic acid since such diets can lead to an increase in the ratio of LDL cholesterol to HDL cholesterol in the blood and tissues[18]. Despite its negative reputation for potential health effects, PA plays crucial roles in several biological functions and its concentration in the body is tightly controlled. Disruptions in PA homeostasis can contribute to various health issues such as atherosclerosis, neurodegenerative diseases, and cancer. However, under normal physiological conditions, the accumulation of PA is prevented through an increase in delta-9 desaturation, leading to the formation of palmitoleic acid (C16:1n9) or elongation to stearic acid (SA, C18:0). This process can continue through additional delta-9 desaturations, resulting in the production of oleic acid (OA, C18:1n9)[17].

Stearic Acid

Stearic acid is a type of long-chain saturated fatty acid that is commonly found in both animal and vegetable fats. It has been shown to have several positive health benefits, such as reducing the spread of metastatic tumors, lowering blood glucose and leptin levels, and reducing visceral fat[19]. Despite this, SA was initially thought to be harmful because it was a saturated fatty

acid which was believed to increase LDL cholesterol and atherosclerosis risk. However, SA does not increase atherosclerosis risk and may even reduce LDL cholesterol. In fact, increased levels of circulating SA are linked to reduced blood pressure, improved heart function, and decreased cancer risk. This suggests that SA has beneficial effects on human health, unlike other saturated fatty acids. However, the molecular mechanisms behind this are not yet understood[20]. In addition, SA has specific roles in metabolism and also complementary roles in dairy cows[21].

Oleic Acid

Studies in recent years have shown the effects of oleic acid on human health and disease. Olive oil, which is rich in OA, is believed to have a modulating effect on various physiological functions, including the immune system. Some studies also suggest that it may have a beneficial effect on cancer, autoimmune and inflammatory diseases, as well as aid in wound healing. The exact role of OA in immune responses is still unclear, but diets containing olive oil may improve the immune response by affecting various components such as macrophages, lymphocytes, and neutrophils. Previous reviews have highlighted the potential role of OA in the development of new therapies for infectious, inflammatory, immune, cardiovascular, and skin diseases[22].

The consumption of a diet rich in olive oil has been linked to reduced incidences of cardiovascular disease and cancer. This is thought to be due to the high content of OA in olive oil. Stearoyl-CoA desaturase 1 (SCD1) is the enzyme responsible for producing OA and for the synthesis of monounsaturated fatty acids (MUFA). The ratio of saturated to monounsaturated fatty acids affects cell growth and differentiation and alterations in this ratio has been implicated

in various diseases. OA represents 49-83% of total fatty acids in olive oil and its consumption has been linked to improved secretory activity in the pancreas and liver, and reduced risk of gastric-duodenal ulcers. MUFAs have been shown to modify plasma lipids and lipoproteins and reduce inflammation, oxidative stress, and coagulation, while improving glucose homeostasis and blood pressure. Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) have stated that OA in olive oil, along with polyphenols, contributes to maintaining normal blood cholesterol levels[23]. The monounsaturated fatty acid OA has been found to have a positive impact on insulin sensitivity, and the dietary PA-to-OA ratio affects diabetes risk in humans[24].

Linoleic Acid

Linoleic acid is an essential nutrient that plays several crucial roles in human health. It is the most commonly consumed polyunsaturated fatty acid (PUFA) in the human diet and is necessary for maintaining the transdermal water barrier of the epidermis. LA functions as a structural component in membrane phospholipids to maintain membrane fluidity and can be enzymatically oxidized for cell signaling[25]. A diet rich in LA has been found to increase reactive oxygen species production, promoting lipid peroxidation[23]. While linoleic acid is necessary for optimal health, excessive production of eicosanoids from arachidonic acid (C20:4n6), which is produced from LA, can contribute to chronic diseases such as inflammation and cancer. Despite this, there is no upper limit set for LA due to a lack of evidence of adverse effects from its consumption in epidemiologic studies. However, exceeding recommended intakes should be

cautiously evaluated as there is limited data available to assess potential negative effects at higher levels. While evidence of ω6 PUFA deficiency is rare in healthy adults, a deficiency in LA can result in skin lesions, growth retardation, and other health problems. Linoleic acid is abundant in many foods such as vegetable oils, nuts, seeds, meats, and eggs. Soybean oil is a major source of LA in the US diet, accounting for 45% of dietary intake, while beans are an exception, with LA comprising 40-50% of the total PUFA. Recent studies have shown that modifying LA intake has little effect on tissue arachidonic acid in humans and that at least 5-10% of energy from LA can reduce the risk of CVD. Additionally, there is little evidence to support the hypothesis that dietary LA promotes inflammation in healthy humans. However, high intake of LA during pregnancy could have negative impacts on fetal development and oxidative stress. The debate over the risks of high LA intake relative to ω3 PUFAs remains an ongoing issue[25].

Adipocyte Lipolysis

Adipocytes, or fat cells, play an important role in the storage and mobilization of fatty acids in the form of TGs in lipid droplets (LDs). Adipocyte lipolysis is the process of breaking down TGs into FAs and glycerol for energy use. FAs can be used for energy or stored as TGs, and they also function as signaling molecules. However, excessive FAs can lead to lipotoxicity and contribute to various metabolic disorders such as inflammation, insulin resistance, and apoptosis. Adipocyte lipolysis is regulated by hormones and protein-protein interactions on the surface of LDs, and lipolysis is catalyzed by three main lipases: PNPLA2/ adipose triglyceride

lipase (ATGL), hormone sensitive lipase (HSL), and monoacylglycerol lipase (MGL). Recent research suggests that lipolysis may not be linear, and many lipolytic proteins have multifunctional roles. Dysregulated lipolysis has been linked to obesity, type 2 diabetes, fatty liver disease, and cancer. The regulation of adipocyte lipolysis and its implications for metabolic disorders are areas of active research[26].

Significance

Sleep is a vital part of human life that is essential for maintaining good health and well-being[27]. According to the American Academy of Sleep Medicine and the Sleep Research Society, adults' recommended sleep duration is at least 7 hours per night. However, over one-quarter of adults had inadequate sleeping time[28]. According to the Centers for Disease Control and Prevention, inadequate sleep prevalence was higher among males than females over years[29]. Insufficient sleep is linked to inflammation in the body, and there are many factors that can affect the quality of sleep, including diet, physical activity, genetics, and the environment[27,30–33]. Insufficient sleep has been associated with several chronic diseases including type 2 diabetes, cardiovascular disease, obesity, depression, and cancer[27,34–38]. Research has found a connection between the quality of carbohydrates consumed and the quality of sleep. A diet high in carbohydrates with a high glycemic index, such as noodles, sweets, and sugary drinks, and the omission of breakfast and irregular meals, is associated with poor sleep. On the other hand, a diet rich in fish, seafood, and vegetables contributes to better sleep quality. The consumption of too few macronutrients, excessive calories, and late meals can reduce sleep quality and may

contribute to the development of insomnia[39]. High energy and fat consumption, binge eating, and nighttime snacking can lead to sleep disorders and disturbances in satiety and hunger. Compared to normal sleepers, people who had inadequate sleep generally have higher energy intake and more high-fat food[40,41]. Eating fatty fish, such as salmon, mackerel, and trout, with more than 5% fat content, has a positive effect on sleep regulation. Fatty fish are rich in omega-3 and omega-6 fatty acids and vitamin D, which can impact the regulation of serotonin secretion and improve sleep quality[42]. In contrast, consuming saturated fatty acids has a negative impact on sleep. Studies have shown that consuming saturated fatty acids leads to more awakenings at night and a shorter duration of slow-wave sleep[43]. In conclusion, a healthy diet that is low in saturated fats and high in fatty fish and vegetables has been shown to contribute to better sleep and overall health.

Study Aims and Hypotheses

Previous studies have concluded that total NEFA was suppressed during sleep restriction and remained suppressed after one night of recovery sleep during a standardized high-fat diet[5]. We are interested in how individual NEFA may respond to a high-fat meal during and after sleep restriction. In this study, saturated (MA, PA, SA), monounsaturated (OA), and polyunsaturated (LA) fatty acids were analyzed. These are included on the basis of quantifiable and reliable measurements due to the increased abundance in adipose tissue in the human body.

Our study has the following aims:

Aim 1: We will quantify how individual NEFA responds to a high-fat meal during sleep restriction.

Hypothesis 1: We hypothesize sleep restriction would suppress individual NEFA concentration during a standardized high-fat dinner (HFD).

Aim 2: We will quantify how individual NEFA responds to a high-fat meal during sleep recovery.

Hypothesis 2: We hypothesize one night of recovery sleep is sufficient to recover the individual NEFA concentration to the baseline value.

Chapter 2 Methods

Participants

This is an ancillary study to a previous study of 15 healthy men ages 22.44 ± 2.82 years, and we randomly selected 4 participants for this study[5]. The prospective participants in this study underwent a physical examination and were excluded for various reasons including previous time zone travel, history of shift work, sleep disorders, current or recent medication, use of tobacco or drug, and ongoing medical disorders. Also, participants were measured for their waist circumference, BMI, seated systolic blood pressure or diastolic blood pressure, HbA1c, HDL, LDL, fasting plasma TGs, and fasting glucose. Participants were advised to refrain from alcohol, narcotics, and caffeine. A urine sample was obtained from the participants for compliance verification upon entry[5].

Design

Before coming to the lab, participants were asked to maintain a 10 h time in bed (TIB) routine for three nights as the baseline condition. In the lab, participants were asked to limit to 5 h TIB for five nights as the restriction condition and two nights of 10 h TIB afterward for the recovery condition. In addition, the lab environment was controlled with light levels, temperature and exposure to their personal electronics before and after 2 hours in bed. Except for specific orders, they were not permitted to sit or recline on the bed during the day and were advised to

remain upright during scheduled wake periods. Also, exercise was limited to only light stretching. The participant's diet was controlled; they were given a high-fat dinner after four consecutive nights with five hours TIB per night. The participants were double-scored by qualified condition-blinded research technicians[5]. Blood samples were collected from these participants after sleep restriction as well as after the recovery period and plasma samples were stored at -80°C.

Plasma samples were stored at the Pennsylvania State University in the lab of Dr. Orfeu Buxton. The stored plasma was extracted using previously described protocols for NEFA analysis[44]. Four of the 25 participants were selected randomly for this ancillary study. We have baseline, sleep restriction and recovery stages. Each visit has 17 time points. We divided them into twelve batches and each batch has 23 samples.

Sample plan preparation

In each batch, we have one blank sample, one surrogate blank sample, three control plasma samples, one matrix spike sample and 17 plasma samples. For the surrogate blank sample, we used 20 ul NEFA surrogate mix. For control plasma samples, we have high, medium and low stages. For the high controlled sample, we combined 400 ul controlled sample and 20 ul NEFA surrogate mix. For the medium controlled sample, we combined 200 ul controlled sample and 20 ul NEFA surrogate mix. For the low controlled sample, we combined 100 ul controlled sample, 100 ul PBS and 20 ul NEFA surrogate mix. For Matrix Spike sample, we combined 200 ul controlled plasma and 10 ul 100% GLC 63C and 20 ul surrogate mix. For the plasma samples, we combined 200 ul plasma and 20 ul surrogate mix.

NEFA extraction and methylation protocol[45]

Fatty acids were extracted with a modified Bligh and Dyer extraction, and NEFA was isolated using solid phase extraction. There are three main steps in this protocol: initial lipid extraction, methylation, and isolation of fame by SPE columns[45].

Initial Lipid Extraction

We first thawed the samples on ice. Then, we mixed the samples with refrigerated hexane and HPLC-grade water with a shaker. After adding refrigerated acetone to each tube, we placed the tubes at -20 °C and centrifuged them at 3000 RPM at 4 °C. Then, we removed the entire acetone and hexane layer and place it in new tubes. NEFA is mostly in this upper layer, so we added hexane and water to new tubes. After shaking them, we centrifuged the samples and placed the supernatant in another new test tube. We kept the previous tubes, added hexane to each tube and place the supernatant in the new test tubes with supernatant[45].

Methylation

The test tubes with supernatant were dried under nitrogen. Then, we added pH 9 buffer and placed it on the shaker. Next was to add hexane, vortex and centrifuge to move the supernatant into clean tubes[45].

Isolation of FAME by SPE

We placed SPE cartridges on the vacuum and washed them with ethyl acetate in hexane and hexane. Then, we put the completed samples into SPE cartridges and washed with hexane. Finally, we washed them with 2% ethyl acetate in hexane and used vials to collect the samples to dry under nitrogen[45].

GC-MS analysis

Before running samples on gas chromatography (GC), we reconstitute using hexane with internal standard (17:1n9) and put it into GC vials.

Peak picking

The size of a peak indicates the quantity of the compound present and can be estimated by treating the peak as a triangle and multiplying its height by half of its width.[46] Quantitative analysis of a component can be carried out by measuring the area of its peak, which enables the determination of the amount of the component present.

After running GC, we got our raw data. Noise is expected and sometimes even appears as a larger area than the real peak. We use the GLC-63c standard concentration as a reference to identify the real peak. We picked peaks for each fatty acid and identify the baseline to quantify the area above the baseline.

Fourteen fatty acids were analyzed. Lauric acid (C12:0), Myristic acid(C14:0), Myristoleic (C14:1), Palmitic acid (C16:0), Palmitoleic acid (C16:1n9), Margaric acid (C17:0), Stearic acid (C18:0), Oleic acid (C18:1n9), Linoleic acid (C18:2n6), alph-Linolenic acid (C18:3n3), gamma-Linolenic acid (C18:3n6), Arachidonic acid (C20:4n6), Eicosapentaenoic acid (C20:5n3), and Docosahexaenoic acid (C22:6n3).

Statistical Methods

We examined the raw data to determine which fatty acids were measured above the limit of detection and able to be quantified. Due to the small sample size, we did not conduct a formal test for normality or complete an outlier analysis. Rather, we examined our data to confirm biologically plausibility. Differences in individual NEFA concentrations at different time points were tested using a mixed-effect linear regression model to analyze within and between group

differences. We used pre-meal baseline concentration for each fatty acid to adjust for between-subject variability. The mixed-effect model predicted NEFA concentration (umol/L) using the sleep condition and sampling time point (minutes) as independent variables. We set our alpha value to 0.1 (due to the small sample size) so $p<0.1$ is considered significant in our study. All analyses were done using JMP Pro 14.0 for modeling and R studio for data visualization.

Chapter 3 Results

Four unidentified, randomly selected participants were chosen from the parent study which included fifteen healthy men (mean ± SD: age 22.33 ± 2.82 years; BMI 24.69 ± 2.99 kg/m2) with an ethnic/racial composition of 60% (n = 9) non-Hispanic white, 20% (n = 3) non-Hispanic black, and 20% (n = 3) Asian[5]. The parent study found no significant differences in total NEFA between age, BMI, and race[5].

For this analysis, myristic acid (MA), palmitic acid (PA), stearic acid (SA), oleic acid (OA), and linoleic acid (LA) are further discussed because they are abundant in adipose tissue in the human body to quantifiable. The NEFA profiles between the sleep conditions prior to the meal and at the expected suppression point (60 min) are not the same (Figure 1). From this figure, we see that PA increased at 60 minutes in both the restriction and recovery compared

with baseline, whereas LA is suppressed only in the baseline and recovery.

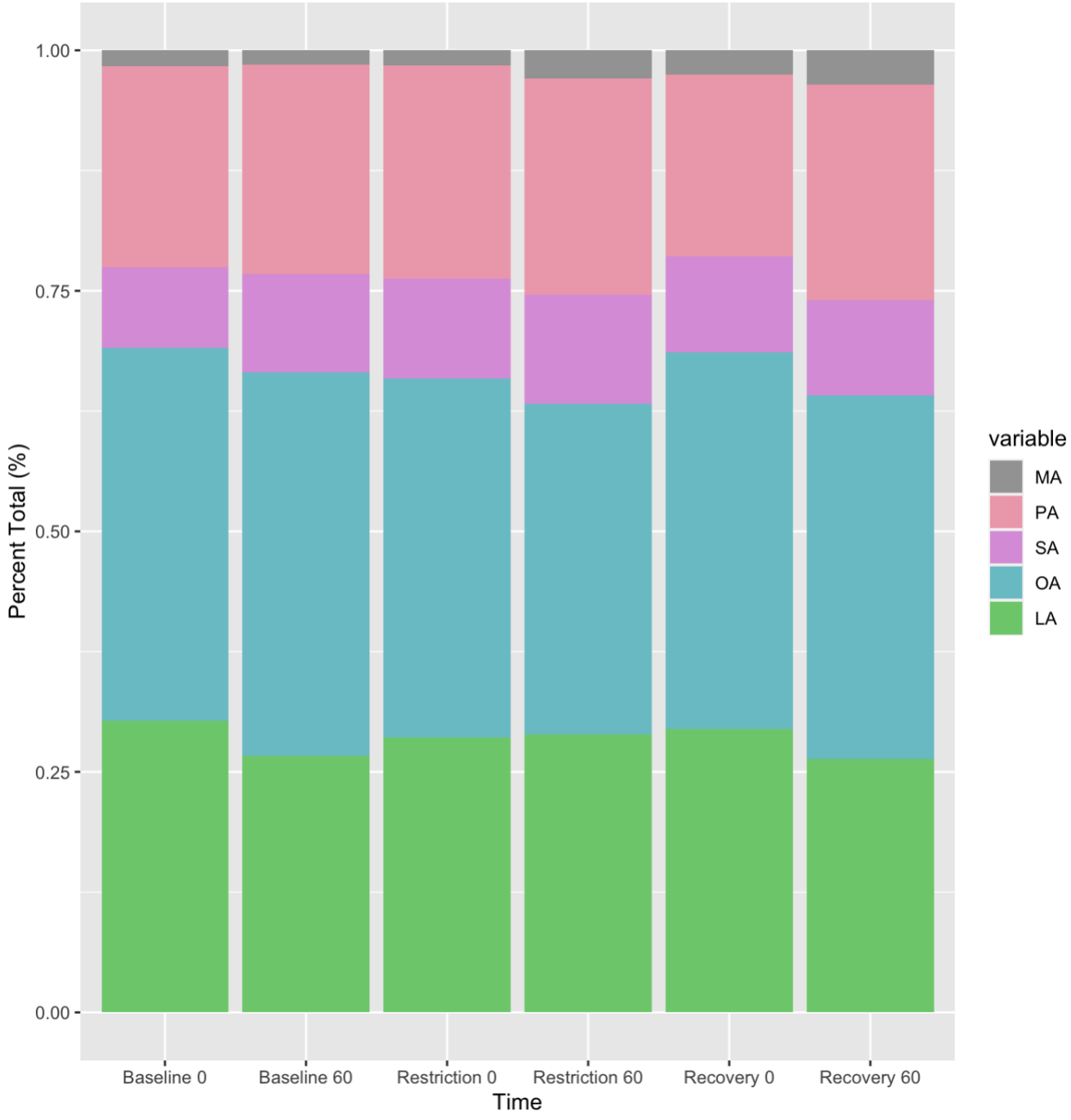

Figure 1: Individual NEFA Percent Total

For figure 2-6 below, the first black dot from the baseline is the fatty acid concentration during fasting. After a high-fat meal, each fatty acid concentration increases for baseline, restriction, and recovery.

Myristic Acid

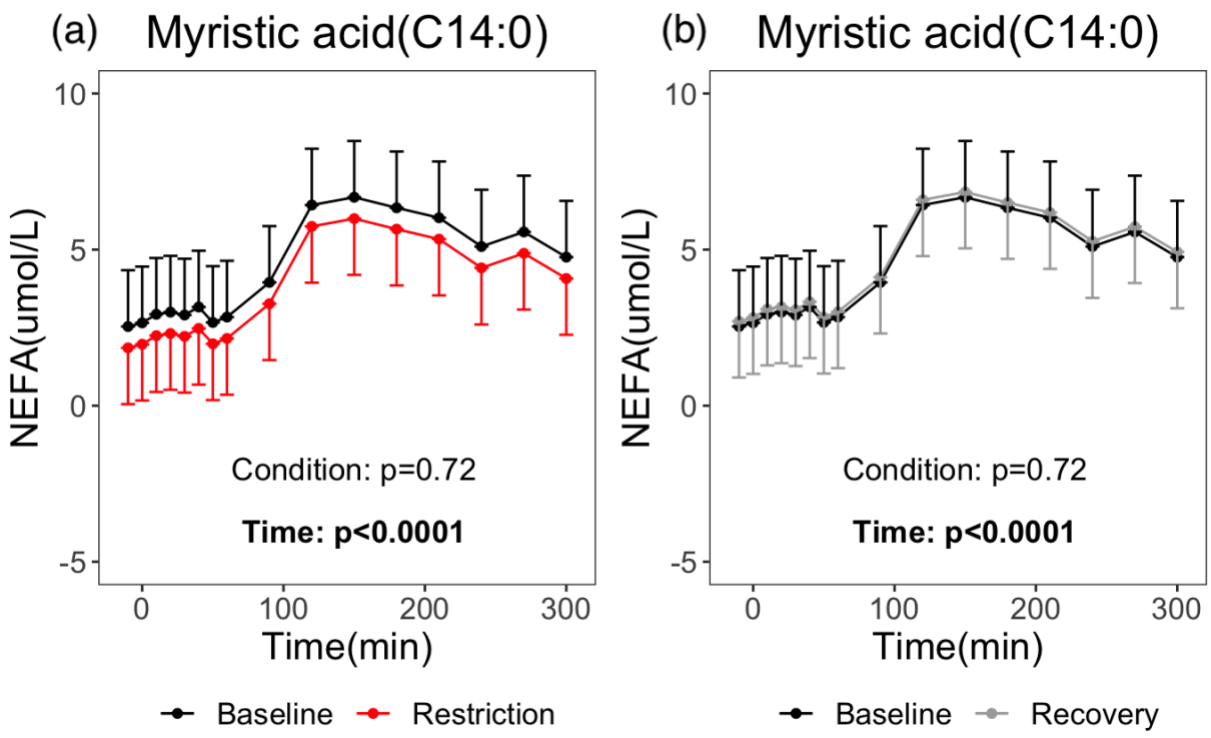

Figure 2: Myristic Acid Visualization

For myristic acid (MA), the sleep condition effect (visit) is not significant (p= 0.72), but the time is significant (p< 0.0001). At the baseline visit, MA has an average estimated concentration of 2.54, 95%CI [0.73, 4.34]. After sleep restriction, MA has an average estimated concentration of 1.85 [0.049, 3.65] before the high-fat meal. After allowed sleep recovery, MA

has an average estimated concentration of 2.70 [0.90, 4.50] before the high-fat meal. For MA, at each visit after the meal, the NEFA concentration dips around 60 minutes and subsequently increases to a peak around 100 minutes. In figure 2 (a) and (b), the time dependent pattern of MA concentration is similar, but the sleep condition has an effect on the average concentration of MA. After sleep restriction, MA is 0.68 [-2.11, 3.48] lower than baseline, however this difference is non-significant (p= 0.81). After allowed recovery, MA is 0.17 [-2.96, 2.63] higher than baseline, however this difference is non-significant (p= 0.99).

Palmitic Acid

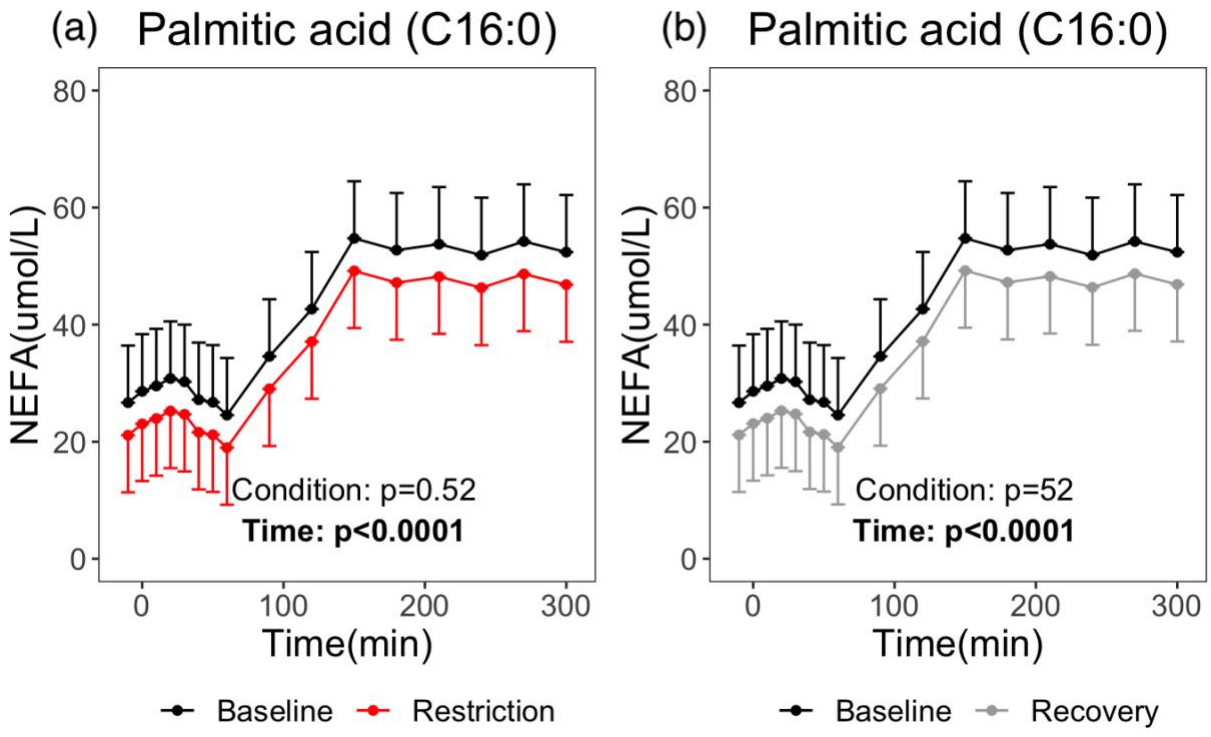

Figure 3: Palmitic Acid Visualization

For palmitic acid (PA), the sleep condition effect (visit) is not significant ($p= 0.52$) and but the time is significant ($p< 0.0001$). At the baseline visit, PA has an average estimated concentration of 26.67, 95%CI [16.91, 36.43]. After sleep restriction, PA has an average estimated concentration of 21.11 [11.35, 30.87] before the high-fat meal. After allowed sleep recovery, PA has an average estimated concentration of 21.17 [11.41, 30.92] before the high-fat meal. For PA, at each visit after the meal, the NEFA concentration dips around 70 minutes and subsequently increases to a peak around 150 minutes. In figure 3 (a) and (b), the time dependent pattern of PA concentration is similar, but the sleep condition has an effect on the average concentration of PA. After sleep restriction, PA is 5.56 [-8.98, 20.10] lower than baseline, however this difference is non-significant ($p= 0.81$). After allowed recovery, PA is 5.51 [-9.03, 20.05] lower than baseline, however this difference is non-significant ($p= 0.58$).

Stearic Acid

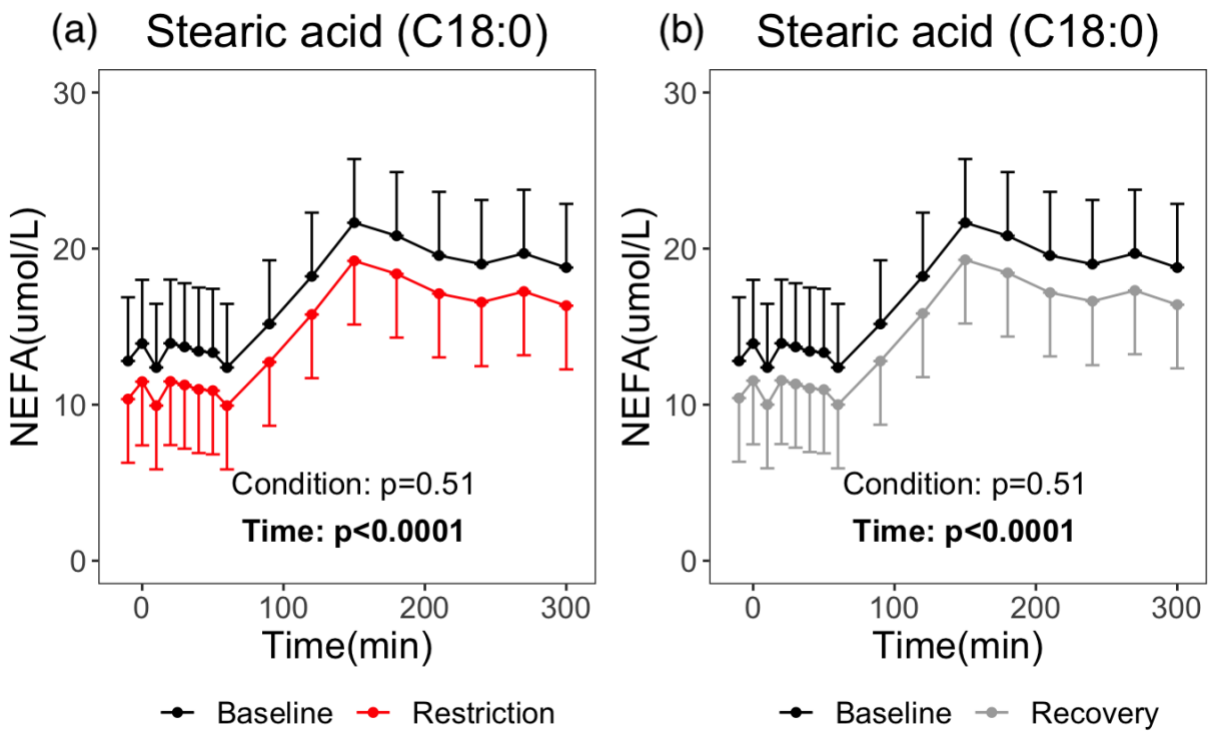

Figure 4: Stearic Acid Visualization

For stearic acid (SA), the sleep condition effect (visit) is not significant (p= 0.51), but the time is significant (p< 0.0001). At the baseline visit, SA has an average estimated concentration of 12.80, 95%CI [8.72, 16.88]. After sleep restriction, SA has an average estimated concentration of 10.36 [6.28, 14.44] before the high-fat meal. After allowed sleep recovery, SA has an average estimated concentration of 10.42 [6.34, 14.50] before the high-fat meal. For SA, at each visit after the meal, the NEFA concentration dips around 70 minutes and subsequently increases to a peak around 150 minutes. In figure 4 (a) and (b), the time dependent pattern of SA concentration is similar, but the sleep condition has an effect on the average concentration of SA. After sleep restriction, SA is 2.44 [-4.24, 9.13] lower than baseline, however this difference is non-

significant (p= 0.56). After allowed recovery, SA is 2.38 [-4.31, 9.06] lower than baseline, however this difference is non-significant (p= 0.58).

Oleic Acid

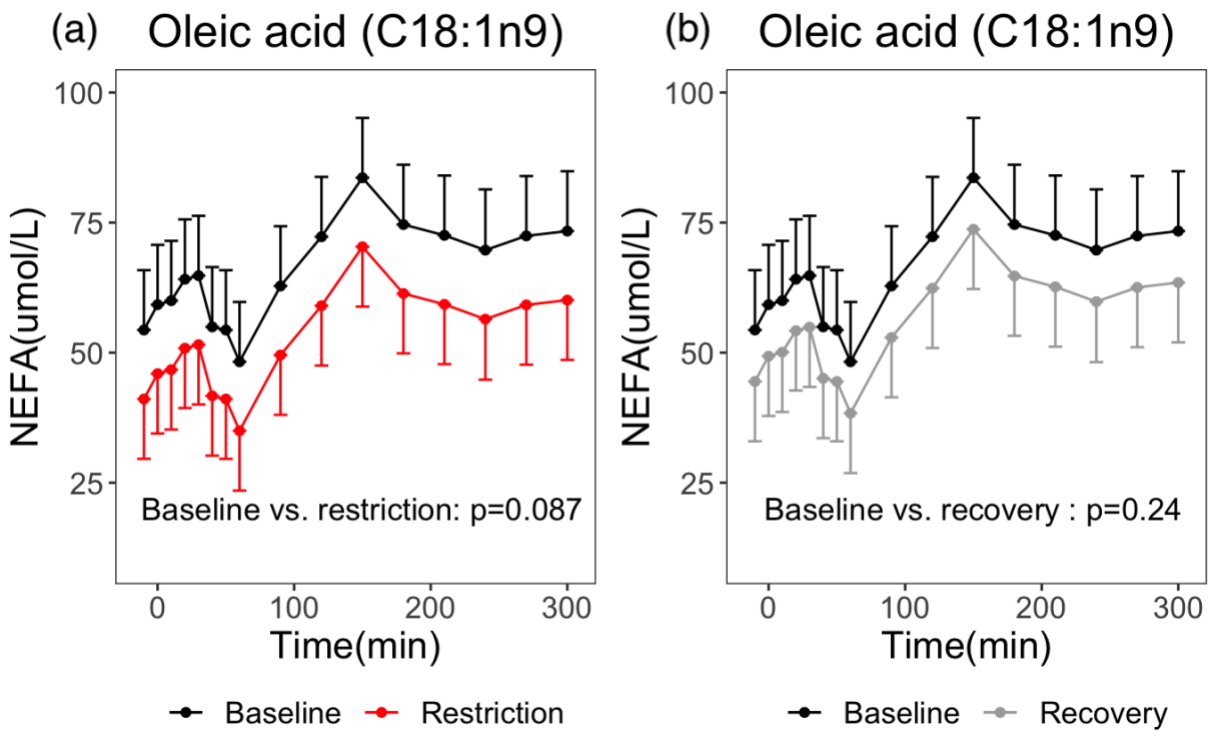

Figure 5: Oleic Acid Visualization

For oleic acid (OA), the sleep condition effect (visit) and time are both significant (p= 0.090, p< 0.0001 respectively). At the baseline visit, OA has an average estimated concentration of 54.36, 95%CI [42.86, 65.85]. After sleep restriction, OA has an average estimated concentration of 41.09 [29.60, 52.58] before the high-fat meal. After allowed sleep recovery, OA has an average estimated concentration of 44.46 [32.97, 55.95] before the high-fat meal. For OA,

at each visit after the meal, the NEFA concentration dips around 75 minutes and subsequently increases to a peak around 150 minutes. In figure 5 (a) and (b), the time dependent pattern of OA concentration is similar, but the sleep condition and time have an effect on the average concentration of OA. After sleep restriction, OA is 13.27 [-1.61, 28.14] lower than baseline and this difference is significant (p= 0.087). After allowed recovery, OA is 9.90 [-4.98, 24.77] lower than baseline, however this difference is non-significant (p= 0.24).

Linoleic Acid

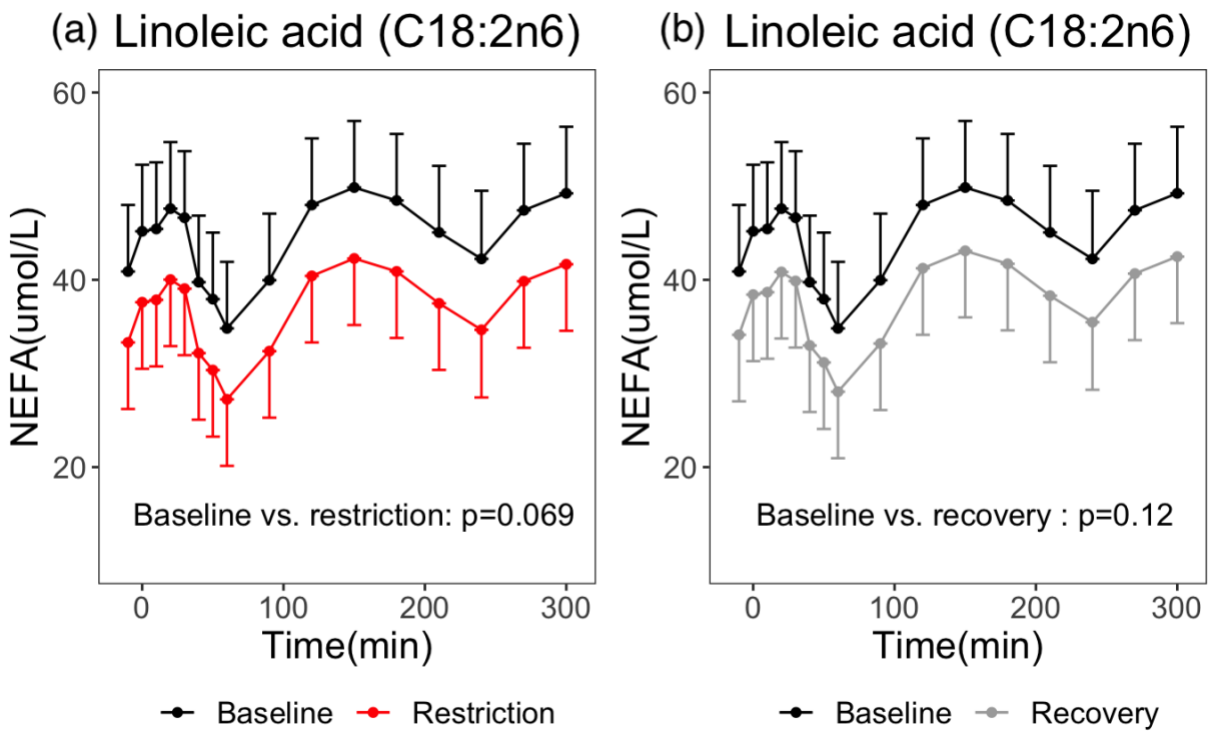

Figure 6: Linoleic Acid Visualization

For linoleic acid (LA), the sleep condition effect (visit) and time are both significant (p= 0.053, p= 0.0012 respectively). At the baseline visit, LA has an average estimated concentration of 40.89, 95%CI [33.78, 47.99]. After sleep restriction, LA has an average estimated concentration of 33.31 [26.21, 40.42] before the high-fat meal. After allowed sleep recovery, LA has an average estimated concentration of 34.13 [27.02, 41.23] before the high-fat meal. For LA, at each visit after the meal, the NEFA concentration dips around 70 minutes and subsequently increases to a peak around 150 minutes. In figure 6 (a) and (b), the time dependent pattern of LA concentration is similar, but the sleep condition and time have an effect on the average concentration of LA. After sleep restriction, LA is 7.58 [-0.48, 15.63] lower than baseline and this difference is significant (p= 0.069). After allowed recovery, LA is 6.76 [-1.30, 14.82] lower than baseline, however this difference is non-significant (p= 0.12).

Chapter 4 Discussion

Findings

This study examined how individual NEFA specifically myristic acid, palmitic acid, stearic acid, oleic acid, and linoleic acid may be suppressed by four nights of 5 h TIB/night by assessing the postprandial response to a standardized high-fat dinner in young healthy men. In addition, this study examined if the individual NEFA can be recovered from one night of recovery sleep (10 h time in bed) to baseline levels during a standardized high-fat dinner in young healthy men. Compared with the baseline value, saturated fatty acids (MA, PA, SA) were not significantly suppressed during sleep restriction. However, compared with the baseline value, unsaturated fatty acids (OA, LA) were significantly suppressed during sleep restriction. All five fatty acids (MA, PA, SA, OA, LA) were not significantly different from the baseline after the allowed sleep recovery.

Sleep is a crucial aspect of human life and overall health. However, over a quarter of adults do not get enough sleep, and men have a higher prevalence of sleep deprivation than women[27–29]. The risks of sleep deprivation are numerous. Studies have linked sleep deprivation to several chronic diseases including type 2 diabetes, cardiovascular disease, obesity, depression, and cancer[27,34–38]. Therefore, it is evident that conducting research on sleep-related topics is necessary. Additionally, we know that diet can impact sleep[27]. Excessive calorie intake at dinner reduces sleep quality and may contribute to the onset of insomnia and these individuals with poorer sleep are more likely to consume foods with higher energy and higher fat contents[39–41].

Previous research showed significant differences in the fatty acid composition among different individual subjects, with notable variations in the proportions of palmitoleic, oleic, and stearic acids at specific locations[47]. A diet with fatty fish which is rich in omega-3 and omega-6 fatty acids can help improve sleep quality[42]. It is worth noting that omega-3 and omega-6 fatty acids are both unsaturated fatty acids[48]. On the other hand, the consumption of saturated fatty acids has negative effects on sleep including more nighttime awakenings and shorter periods of slow-wave sleep[43]. Considering the fatty acids in our study which are focusing on, MA, PA, and SA (saturated fatty acids), and OA and LA (unsaturated fatty acids), only the concentration of OA and LA was significantly suppressed compared to the baseline during sleep restriction. None of the fatty acids fully recovered after allowed recovery, indicating that our body cannot recover from NEFA concentration in a short-term period after sleep restriction.

NEFA is acknowledged as a risk factor for cardiovascular diseases and is strongly associated with metabolic syndromes including obesity and type 2 diabetes[49,50]. Research has shown NEFA not only plays an important role in causing insulin resistance but also triggers inflammatory reactions in liver and skeletal muscle tissues that are targeted by insulin[50,51,52,53]. Thus, raising NEFA in the bloodstream is considered to be connected with insulin resistance, inflammation, obesity, type 2 diabetes and hypertension[50]. Moreover, previous studies have reported an elevation of NEFA might be related to lung cancer, breast cancer, and early-stage detection of colorectal cancer[54-55.] While the parent study provided valuable insights, it only measured the total NEFA, without delving into each individual NEFA[5]. It's important to understand each individual NEFA since they all have their own characteristics and functions that are worth investigating. By examining individual NEFA, we can gain a deeper understanding of their specific roles and effects within the body. MA has potential association with metabolic

disorders and cardiovascular disease, and high levels in serum triglycerides have been linked with obesity and metabolic problems[9,18]. The negative reputation of PA is due to its potential to increase the risk of cardiovascular disease, but it plays crucial roles in several biological functions[17,18]. SA was initially thought to be harmful because it was saturated fatty acid but after further investigation, SA has been shown some positive health benefits, including slowing the spread of metastatic tumors, lowering blood glucose and leptin levels, and reducing visceral fat. It does not increase atherosclerosis risk and may even reduce LDL cholesterol[19,20]. OA has been linked to potential benefits for the immune system, cancer, autoimmune and inflammatory diseases, wound healing, and various physiological functions. Additionally, OA is believed to contribute to maintaining normal blood cholesterol levels and improving insulin sensitivity[22-24]. LA is essential for maintaining the transdermal water barrier of the epidermis, cell signaling, and membrane fluidity[25]. A diet rich in LA may increase reactive oxygen species production, promoting lipid peroxidation, and excessive production of eicosanoids from arachidonic acid (produced from LA) can contribute to chronic diseases such as inflammation and cancer[23,25]. A deficiency in LA can result in skin lesions, growth retardation, and other health problems[23,25]. Each fatty acid warrants continued investigation.

Compared to unsaturated fatty acids (OA, LA), sleep restriction has less suppression of saturated fatty acids (MA, PA, SA) in response to high-fat meals which means there are more circulating saturated fatty acids in the body. In addition, the allowed recovery (one night) doesn't improve the previous suppression for all fatty acids (PA, MA, SA, OA, LA) which means the participants are not able to remove fatty acids from their blood into storage efficiently so that the participants still have higher circulating fatty acids. Circulating fatty acids have been considered associate with obesity, inflammation, insulin resistance, type 2 diabetes (T2D), and

hypertension[50]. Elevated plasma NEFA level is commonly found in obese individuals[56]. If the participants are not able to respond to glucose, it might lead to insulin resistance. Elevating plasma NEFA level will increase insulin resistance while decreasing NEFA level will improve insulin resistance[57,58]. Additionally, previous research demonstrated circulating fatty acids can influence total cholesterol and lipoprotein cholesterol concentrations, thus making the circulating fatty acids serve as an indicator to help detect risks of cardiovascular diseases[59]. Some research suggests that circulating fatty acids may have negative effects on metabolic health. However, there are conflicting results, which suggest that there is insufficient evidence on the relationship between circulating fatty acid levels, obesity and insulin resistance[60]. Moreover, there is no clear evidence about the association between circulating fatty acid and type 2 diabetes[61,62].

Strengths and Limitation

There are some valuable strengths of this study. The participants were carefully selected based on multiple biomarker-based measures rather than self-reported health status, allowing for the identification of even subtle differences with smaller sample sizes. Our human plasma samples were collected in a controlled environment, with variables such as lab environment, exercise level, diet, and bed time being monitored. This attention to detail allowed for a higher degree of confidence in the manipulation, which in turn resulted in greater validity of the results. By using controlled experiments, we were able to increase the reliability and generalizability of the findings. In addition, the samples were collected meticulously at numerous time points, enabling a thorough analysis of the data. Additionally, the analysis of individual NEFA provides

deeper insight into the specific metabolism and response of this bioactive metabolites during sleep restriction and recovery.

The study has certain limitations due to the small size of the sample and the population group being only healthy males, which narrows its applicability to a broader population. In the future, it is recommended to expand the scope of participants to include different genders and different age groups, as well as consider a longer recovery period. For the recovery period specifically, we cannot ensure that the participants were able to sleep the exact amount of time (10 hrs), potentially impacting the extent to which their cognitive and physiological functioning returned to baseline levels. Furthermore, we did not assess the potential impact of the restricted sleep on the participants' mental health, which could have been an important consideration given the potential negative effects of sleep deprivation.

Conclusion

The rate of inadequate sleep continues to increase, and understanding the important role of fatty acids in this challenge is crucial for improving human health and disease prevention. Our study found that during HFD, saturated fatty acids (MA, PA, SA) were not significantly suppressed during sleep restriction, while unsaturated fatty acids (OA, LA) were significantly suppressed. However, after allowed recovery, the five fatty acids (MA, PA, SA, OA, LA) were not significantly different from the baseline. We found sleep restriction inhibited normal suppression of unsaturated, but not saturated, fatty acids in response to a HFD which was

restored after allowed sleep recovery. Future studies are needed to further understand individual NEFA metabolism in sleep restriction and the consequences for health.

BIBLIOGRAPHY

1. Kimura I, Ichimura A, Ohue-Kitano R, Igarashi M. Free Fatty Acid Receptors in Health and Disease. Physiol Rev. 2020;100(1):171-210. doi:10.1152/physrev.00041.2018

2. Karpe F, Dickmann JR, Frayn KN. Fatty Acids, Obesity, and Insulin Resistance: Time for a Reevaluation. Diabetes. 2011;60(10):2441-2449. doi:10.2337/db11-0425

3. Stich V, Berlan M. Physiological regulation of NEFA availability: lipolysis pathway. Proceedings of the Nutrition Society. 2004;63(2):369-374. doi:10.1079/PNS2004350

4. Frayn KN. Non-esterified fatty acid metabolism and postprandial lipaemia. Atherosclerosis. 1998;141 Suppl 1:S41-46. doi:10.1016/s0021-9150(98)00216-0

5. Ness KM, Strayer SM, Nahmod NG, et al. Four nights of sleep restriction suppress the postprandial lipemic response and decrease satiety. J Lipid Res. 2019;60(11):1935-1945. doi:10.1194/jlr.P094375

6. Randle Cycle - an overview | ScienceDirect Topics. Accessed February 1, 2023. https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/randle-cycle

7. Jensen MD. Adipose tissue and fatty acid metabolism in humans. J R Soc Med. 2002;95(Suppl 42):3-7.

8. Sex Differences in Visceral Fat Lipolysis and Metabolic Complications of Obesity | Arteriosclerosis, Thrombosis, and Vascular Biology. Accessed March 11, 2023. https://www.ahajournals.org/doi/full/10.1161/01.ATV.17.7.1472

9. Saraswathi V, Kumar N, Ai W, et al. Myristic Acid Supplementation Aggravates High Fat Diet-Induced Adipose Inflammation and Systemic Insulin Resistance in Mice. Biomolecules. 2022;12(6):739. doi:10.3390/biom12060739

10. Chiappini F, Desterke C, Bertrand-Michel J, Guettier C, Le Naour F. Hepatic and serum lipid signatures specific to nonalcoholic steatohepatitis in murine models. Sci Rep. 2016;6:31587. doi:10.1038/srep31587

11. Puri P, Wiest MM, Cheung O, et al. The Plasma Lipidomic Signature of Nonalcoholic Steatohepatitis. Hepatology. 2009;50(6):1827-1838. doi:10.1002/hep.23229

12. Chiappini F, Coilly A, Kadar H, et al. Metabolism dysregulation induces a specific lipid signature of nonalcoholic steatohepatitis in patients. Sci Rep. 2017;7:46658. doi:10.1038/srep46658

13. Udenwobele DI, Su RC, Good SV, Ball TB, Varma Shrivastav S, Shrivastav A. Myristoylation: An Important Protein Modification in the Immune Response. Front Immunol. 2017;8:751. doi:10.3389/fimmu.2017.00751

14. Rioux V, Pédrono F, Legrand P. Regulation of mammalian desaturases by myristic acid: N-terminal myristoylation and other modulations. Biochim Biophys Acta. 2011;1811(1):1-8. doi:10.1016/j.bbalip.2010.09.005

15. Perreault M, Zulyniak MA, Badoud F, et al. A Distinct Fatty Acid Profile Underlies the Reduced Inflammatory State of Metabolically Healthy Obese Individuals. PLoS One. 2014;9(2):e88539. doi:10.1371/journal.pone.0088539

16. Masquio DCL, de Piano-Ganen A, Oyama LM, et al. The role of free fatty acids in the inflammatory and cardiometabolic profile in adolescents with metabolic syndrome engaged in interdisciplinary therapy. J Nutr Biochem. 2016;33:136-144. doi:10.1016/j.jnutbio.2016.03.017

17. Carta G, Murru E, Banni S, Manca C. Palmitic Acid: Physiological Role, Metabolism and Nutitional Implications. Front Physiol. 2017;8:902. doi:10.3389/fphys.2017.00902

18. Kien CL, Bunn JY, Stevens R, et al. Dietary intake of palmitate and oleate has broad impact on systemic and tissue lipid profiles in humans123. Am J Clin Nutr. 2014;99(3):436-445. doi:10.3945/ajcn.113.070557

19. Shen MC, Zhao X, Siegal GP, Desmond R, Hardy RW. Dietary Stearic Acid Leads to a Reduction of Visceral Adipose Tissue in Athymic Nude Mice. PLoS ONE. 2014;9(9). doi:10.1371/journal.pone.0104083

20. Senyilmaz-Tiebe D, Pfaff DH, Virtue S, et al. Dietary stearic acid regulates mitochondria in vivo in humans. Nat Commun. 2018;9:3129. doi:10.1038/s41467-018-05614-6

21. Loften JR, Linn JG, Drackley JK, Jenkins TC, Soderholm CG, Kertz AF. Invited review: palmitic and stearic acid metabolism in lactating dairy cows. J Dairy Sci. 2014;97(8):4661-4674. doi:10.3168/jds.2014-7919

22. Sales-Campos H, Souza PR de, Peghini BC, da Silva JS, Cardoso CR. An overview of the modulatory effects of oleic acid in health and disease. Mini Rev Med Chem. 2013;13(2):201-210.

23. Piccinin E, Cariello M, De Santis S, et al. Role of Oleic Acid in the Gut-Liver Axis: From Diet to the Regulation of Its Synthesis via Stearoyl-CoA Desaturase 1 (SCD1). Nutrients. 2019;11(10):2283. doi:10.3390/nu11102283

24. Palomer X, Pizarro-Delgado J, Barroso E, Vázquez-Carrera M. Palmitic and Oleic Acid: The Yin and Yang of Fatty Acids in Type 2 Diabetes Mellitus. Trends in Endocrinology & Metabolism. 2018;29(3):178-190. doi:10.1016/j.tem.2017.11.009

25. Whelan J, Fritsche K. Linoleic Acid1. Adv Nutr. 2013;4(3):311-312. doi:10.3945/an.113.003772

26. Yang A, Mottillo EP. Adipocyte Lipolysis: from molecular mechanisms of regulation to disease and therapeutics. Biochem J. 2020;477(5):985-1008. doi:10.1042/BCJ20190468

27. Sejbuk M, Mirończuk-Chodakowska I, Witkowska AM. Sleep Quality: A Narrative Review on Nutrition, Stimulants, and Physical Activity as Important Factors. Nutrients. 2022;14(9):1912. doi:10.3390/nu14091912

28. Sleep Difficulties in Adults: United States, 2020. Accessed February 1, 2023. https://stacks.cdc.gov/view/cdc/117490

29. Adults - Sleep and Sleep Disorders | CDC. Accessed January 31, 2023. https://www.cdc.gov/sleep/data-and-statistics/adults.html

30. Ageborg Morsing J, Smith MG, Ögren M, et al. Wind Turbine Noise and Sleep: Pilot Studies on the Influence of Noise Characteristics. Int J Environ Res Public Health. 2018;15(11):2573. doi:10.3390/ijerph15112573

31. Saidi O, Rochette E, Doré É, et al. Randomized Double-Blind Controlled Trial on the Effect of Proteins with Different Tryptophan/Large Neutral Amino Acid Ratios on Sleep in Adolescents: The PROTMORPHEUS Study. Nutrients. 2020;12(6):1885. doi:10.3390/nu12061885

32. Murawski B, Plotnikoff RC, Rayward AT, Vandelanotte C, Brown WJ, Duncan MJ. Randomised controlled trial using a theory-based m-health intervention to improve physical activity and sleep health in adults: the Synergy Study protocol. BMJ Open. 2018;8(2):e018997. doi:10.1136/bmjopen-2017-018997

33. Dashti HS, Jones SE, Wood AR, et al. Genome-wide association study identifies genetic loci for self-reported habitual sleep duration supported by accelerometer-derived estimates. Nat Commun. 2019;10:1100. doi:10.1038/s41467-019-08917-4

34. Zhai L, Zhang H, Zhang D. SLEEP DURATION AND DEPRESSION AMONG ADULTS: A META-ANALYSIS OF PROSPECTIVE STUDIES. Depress Anxiety. 2015;32(9):664-670. doi:10.1002/da.22386

35. Role of sleep duration and quality in the risk and severity of type 2 diabetes mellitus - PubMed. Accessed February 1, 2023. https://pubmed.ncbi.nlm.nih.gov/16983057/

36. Kasasbeh E, Chi DS, Krishnaswamy G. Inflammatory aspects of sleep apnea and their cardiovascular consequences. South Med J. 2006;99(1):58-67; quiz 68-69, 81. doi:10.1097/01.smj.0000197705.99639.50

37. Taheri S. The link between short sleep duration and obesity: we should recommend more sleep to prevent obesity. Arch Dis Child. 2006;91(11):881-884. doi:10.1136/adc.2005.093013

38. Yu J, Rawtaer I, Fam J, et al. Sleep correlates of depression and anxiety in an elderly Asian population. Psychogeriatrics. 2016;16(3):191-195. doi:10.1111/psyg.12138

39. Binks H, E. Vincent G, Gupta C, Irwin C, Khalesi S. Effects of Diet on Sleep: A Narrative Review. Nutrients. 2020;12(4):936. doi:10.3390/nu12040936

40. Grandner MA, Kripke DF, Naidoo N, Langer RD. Relationships among dietary nutrients and subjective sleep, objective sleep, and napping in women. Sleep Med. 2010;11(2):180. doi:10.1016/j.sleep.2009.07.014

41. St-Onge MP, Mikic A, Pietrolungo CE. Effects of Diet on Sleep Quality. Advances in Nutrition. 2016;7(5):938-949. doi:10.3945/an.116.012336

42. Lavialle M, Champeil-Potokar G, Alessandri JM, et al. An (n-3) polyunsaturated fatty acid-deficient diet disturbs daily locomotor activity, melatonin rhythm, and striatal dopamine in Syrian hamsters. J Nutr. 2008;138(9):1719-1724. doi:10.1093/jn/138.9.1719

43. St-Onge MP, Roberts A, Shechter A, Choudhury AR. Fiber and Saturated Fat Are Associated with Sleep Arousals and Slow Wave Sleep. J Clin Sleep Med. 2016;12(1):19-24. doi:10.5664/jcsm.5384

44. Walker RE, Ford JL, Boston RC, et al. Trafficking of nonesterified fatty acids in insulin resistance and relationship to dysglycemia. Am J Physiol Endocrinol Metab. 2020;318(3):E392-E404. doi:10.1152/ajpendo.00331.2019

45. Bligh EG, Dyer WJ. A rapid method of total lipid extraction and purification. Can J Biochem Physiol. 1959;37(8):911-917. doi:10.1139/o59-099

46. Gas Chromatography: Calculating the Area. Accessed February 20, 2023. https://www.chemedx.org/JCESoft/jcesoftSubscriber/ChemPagesLab/modules/gaschrom/gaschromcalc.htm

47. Calder PC, Harvey DJ, Pond CM, Newsholme EA. Site-specific differences in the fatty acid composition of human adipose tissue. Lipids. 1992;27(9):716-720. doi:10.1007/BF02536031

48. The importance of omega-3 and omega-6 fatty acids. Accessed March 16, 2023. https://www.eufic.org/en/whats-in-food/article/the-importance-of-omega-3-and-omega-6-fatty-acids

49. Nonesterified fatty acids in blood pressure control and cardiovascular complications - ProQuest. Accessed March 19, 2023. https://www.proquest.com/openview/4bb2be49b6d7c00e8b8bb71e9cddbc7c/1?cbl=326347&pq-origsite=gscholar&parentSessionId=ljXKzJqpfnqmop%2F12meK2G7DCHPU4rLX%2BSBoM6rgQI8%3D

50. Boden G. Obesity and Free Fatty Acids. Endocrinology and Metabolism Clinics of North America. 2008;37(3):635-646. doi:10.1016/j.ecl.2008.06.007

51. Capurso C, Capurso A. From excess adiposity to insulin resistance: The role of free fatty acids. Vascular Pharmacology. 2012;57(2):91-97. doi:10.1016/j.vph.2012.05.003

52. Delarue J, Magnan C. Free fatty acids and insulin resistance. Current Opinion in Clinical Nutrition & Metabolic Care. 2007;10(2):142. doi:10.1097/MCO.0b013e328042ba90

53. Haus JM, Solomon TPJ, Marchetti CM, Edmison JM, González F, Kirwan JP. Free Fatty Acid-Induced Hepatic Insulin Resistance is Attenuated Following Lifestyle Intervention in Obese Individuals with Impaired Glucose Tolerance. The Journal of Clinical Endocrinology & Metabolism. 2010;95(1):323-327. doi:10.1210/jc.2009-1101

54. Liu J, Mazzone PJ, Cata JP, et al. Serum Free Fatty Acid Biomarkers of Lung Cancer. Chest. 2014;146(3):670-679. doi:10.1378/chest.13-2568

55. Zhang Y, He C, Qiu L, et al. Serum Unsaturated Free Fatty Acids: A Potential Biomarker Panel for Early-Stage Detection of Colorectal Cancer. J Cancer. 2016;7(4):477-483. doi:10.7150/jca.13870

56. Measurement of Plasma Glucose, Free Fatty Acid, Lactate, and Insulin for 24 h in Patients With NIDDM | Diabetes | American Diabetes Association. Accessed March 19, 2023. https://diabetesjournals.org/diabetes/article/37/8/1020/7334/Measurement-of-Plasma-Glucose-Free-Fatty-Acid

57. Boden G, Chen X, Ruiz J, White JV, Rossetti L. Mechanisms of fatty acid-induced inhibition of glucose uptake. J Clin Invest. 1994;93(6):2438-2446. doi:10.1172/JCI117252

58. Overnight lowering of free fatty acids with Acipimox improves insulin resistance and glucose tolerance in obese diabetic and nondiabetic subjects. | Diabetes | American Diabetes Association. Accessed March 19, 2023.

https://diabetesjournals.org/diabetes/article/48/9/1836/10644/Overnight-lowering-of-free-fatty-acids-with

59. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. Arteriosclerosis and Thrombosis: A Journal of Vascular Biology. 1992;12(8):911-919. doi:10.1161/01.ATV.12.8.911

60. Bi X, Yeo PLQ, Loo YT, Henry CJ. Associations between circulating fatty acid levels and metabolic risk factors. Journal of Nutrition & Intermediary Metabolism. 2019;15:65-69. doi:10.1016/j.jnim.2019.02.002

61. Huang L, Lin J sheng, Aris IM, Yang G, Chen WQ, Li LJ. Circulating Saturated Fatty Acids and Incident Type 2 Diabetes: A Systematic Review and Meta-Analysis. Nutrients. 2019;11(5):998. doi:10.3390/nu11050998

62. Wu JHY, Marklund M, Imamura F, et al. Omega-6 fatty acid biomarkers and incident type 2 diabetes: pooled analysis of individual-level data for 39 740 adults from 20 prospective cohort studies. The Lancet Diabetes & Endocrinology. 2017;5(12):965-974. doi:10.1016/S2213-8587(17)30307-8

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