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Early-Day Protein Intake Influences the Transition of Metabolic Health Phenotypes among Adults with Obesity

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Abstract

Metabolically healthy obesity (MHO) represents a subset of obesity characterized by a lower risk of cardiometabolic syndrome than individuals with metabolically unhealthy obesity (MUO). This study aimed to (1) describe the transition of metabolic health phenotypes in adults with obesity and (2) identify the differentiating factors associated with this transition following the 12-week weight reduction program. This study recruited 91 adults with obesity (Age: 39.6±6.3 years; 74.7% women; body mass index (BMI): 31.2±4.5 kg/m^2). The weight reduction intervention incorporates multiple lifestyle domains, including dietary modifications, physical activity, behavioural strategies, and chrono-nutrition, which encompasses temporal eating patterns, meal timing and sleep. At pre-intervention, 55% of participants (n=50) were classified as MHO: BMI≥25kg/m^2 with fewer than three metabolic abnormalities, while 45% (n=41) were classified as MUO: BMI≥25kg/m^2 with three or more metabolic abnormalities. Post-intervention, about 24% of the participants (n=22) exhibited positive changes, transitioning from MUO to MHO or from MUO/MHO to metabolically healthy normal weight (MHN). The MUO proportion decreased to 31% (n=28), and 45% (n=41) remained as MHO. Participants who demonstrated positive changes were characterized with highest increase in energy intake from protein sources (+5.2% vs +1.1%, p=0.004), particularly during the earlier part of the day (+4.3% vs +1.1%, p=0.029), greater body weight loss (-7.0% vs -3.2%, p=0.022), body fat loss (-3.4% vs -1.3%, p=0.013) and visceral fat loss (-1.3 vs -0.5, p=0.013) as well as a higher proportion of morning chronotype (72.7% vs 35.7%, p=0.033),

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than the participants who showed negative changes. These results imply that, the timing of protein intake and chronotype may play significant roles in mitigating the risk of cardiometabolic syndrome among adults with obesity, in addition to weight reduction.

Introduction

Obesity has emerged as a global health crisis due to the excessive accumulation of body fat, which has a detrimental impact on the metabolic health of individuals. A multitude of factors contribute to obesity, including dietary factors such as the overconsumption of energy-dense foods and limited physical activity.[1] The prevalence of obesity has skyrocketed worldwide, reaching pandemic proportions and posing a formidable public health challenge.[2,3] The World Health Organization (WHO) reports that the prevalence of obesity worldwide has almost tripled since 1975. The WHO predicts that by 2025, an estimated 167 million people, including both adults and children, will become less healthy due to obesity or being overweight.[4]

Metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO) are two distinct phenotypes that have garnered significant attention in recent research.[5,6] MHO is characterized by the presence of obesity in the absence of metabolic disturbances, such as hypertension, impaired glycaemic control, systemic inflammation, adverse lipid profiles, and insulin resistance.[2] Conversely, MUO refers to obese individuals who exhibit these metabolic abnormalities.[7] This concept of metabolic health state has emerged as critical area of research in the context of obesity. The definition of MHO has been a subject of debate due to the need for more consensus. However, it is generally agreed that individuals with MHO may have a more favourable fat distribution, lower visceral fat, and a more favourable inflammatory profile compared to their MUO counterparts.[3,8]

Cross-sectional studies has reported that MUO was associated with poorer dietary intake patterns and less healthy lifestyle compared to MHO individuals.[3,5] A recent study conducted among Japanese males discovered that MHO individual had greater physical activity expenditure than MUO individual.[3] Previously, we also demonstrated potential modifiable risk factors for being classified as MUO in a cross-sectional association study5. Nonetheless, few research has investigated the transition of metabolic health phenotypes and the dietary factors that may influence this transition. Hence, in this current study, we aimed to (1) describe the transition of metabolic health phenotypes adults with obesity who do not work shifts and (2) identify the differentiating factors associated with this transition following the weight reduction program. Despite the increasing prevalence of obesity and the recognition of MHO and MUO, there is a lack of comprehensive studies investigating these transitions and their influencing factors. Therefore, this study is needed to fill this gap in the literature and contribute to the development of more effective obesity management strategies. The findings of this study could have significant implications for public health policies and individualized treatment plans for obesity.

Materials and Methods

Study Design

This study is a secondary data analysis of a quasi-experimental weight reduction intervention study among non-shift workers with obesity at Klang Valley, an urbanized region in the heart of Malaysia.[9] The 12-week weight reduction intervention was carried out from October 2019 to December 2019, weekly session. The weight reduction intervention incorporates multiple lifestyle domains, including dietary modifications, physical activity, behavioural strategies, and chrono-nutrition, which encompasses temporal eating patterns, meal timing and sleep. Participants were prescribed daily energy intakes of 1,600 to 1,800 kcal for men and 1,200 to 1,500 kcal for women. In terms of chrono-nutrition component, energy intake distribution was tailored to each participant's chronotype – morning and evening chronotype. Specifically, those with a morning chronotype received a greater proportion of energy intake earlier in the day, compared to those with an evening chronotype. Details of dietary prescription and intervention framework has been described in a previous publication.[9]

The criteria for inclusion in this study are adults aged 20-59 years old with a body mass index (BMI) of 25.0 kg/m^2 or higher, who reside and work in Putrajaya, have non-shift employment, and do not suffer from the following chronic diseases; cancer, renal disease, or heart disease. Additionally, participants should be at least in the contemplation stage of behaviour change. The exclusion criteria for this study include pregnant or lactating mothers, individuals with uncontrolled diabetes or hypertension, current recipients of bariatric surgery, those consuming any medications or weight loss products, individuals with a diagnosis of chronic disease, engaged in any kind of weight loss program in the last three months, and those with serious joint problems.

The sample size calculation is detailed in a previous publication.[9] Briefly, the sample size was determined using GPower version 3.1, based on the effect size from a prior study, with an alpha level of 0.05, 80% power, and a 20% anticipated dropout rate, resulting in a target of 105 participants. All participants provided informed consent, and this research was done in line with the Declaration of Helsinki and authorized by the Research and Ethical Committee of Medical Research of Universiti Kebangsaan Malaysia (UKM PPI/111/8/JEP- 2017-656).

Transition of Metabolic Health Phenotypes

The classification of metabolic heath phenotypes was based on the five cardiometabolic syndrome which is (1) a fasting blood glucose level of at least 5.6 mmol/L, or the use of diabetic medication; (2) fasting triglycerides of at least 1.7 mmol/L, or medication; (3) fasting HDL-C levels below 1.29 mmol/L for women and below 1.03 mmol/L for men; (4) waist circumference of at least 80 cm for women and at least 90 cm for men; and (5) blood pressure with a systolic pressure of at least 130 mmHg and a diastolic pressure of at least 85 mmHg, or the use of antihypertensive medication.[10] Metabolically healthy obesity (MHO) was defined as having no more than two of the five metabolic syndrome components, whereas metabolically unhealthy obesity (MUO) was characterized by the presence of three or more of these components.[11]

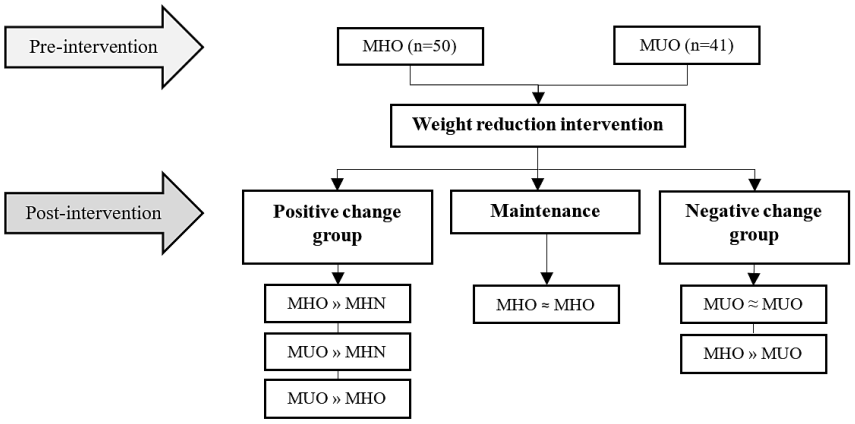

Fig.1 Transition in metabolic health phenotypes. At pre-intervention, participants were categorized into MHO and MUO groups. Post-intervention, transitions in metabolic health phenotypes was observed and participants were subsequently classified into positive change, maintenance or negative change groups based on changes in their metabolic health. Abbreviation: MHO, metabolically healthy obesity; MHN, metabolically healthy normal weight; MUO; metabolically unhealthy obesity.

Following the weight reduction intervention, a transition in metabolic health phenotypes was observed, resulting in positive, maintenance or negative changes (Figure 1). The positive change group included participants who transitioned from MUO or MHO to metabolically healthy normal weight (MHN). The maintenance group consisted of MHO participants whose metabolic status remained unchanged after the intervention. In contrast, the negative change group comprised participants who transitioned from MHO to MUO or remained in the MUO state.

Sociodemographic Background

Before the intervention program, the following variables were determined: age, sex, ethnicity, educational background, marital status, monthly household income, and self-reported medical conditions.

Adiposity Parameter

Adiposity was analysed using bioelectrical impedance for body weight and body fat (TANITA DC-360, Tanita Corporation of America, Arlington Heights, IL, USA), to the nearest 0.1 kg. Height was assessed using a stadiometer (Seca 213, Hamburg, Germany).

Dietary Intake and Temporal Eating Pattern

A validated dietary history questionnaire assessed participants' dietary consumption.[12] This tool also facilitated the determination of chrono-nutrition habits, include meal timing and temporal pattern of energy and macronutrients intake. Qualified dietitians and nutritionists conducted the interviews. The data were assessed using Nutritionist Pro Software and the Malaysian Food Composition Database. The temporal pattern of energy intake was assessed based on the midpoint of eating timing.[9] The midpoint of eating represents the midpoint between the first and last mealtime. Thus, the eating window was categorized into an early window, encompassing meals consumed before the midpoint of eating, and a late window, including meals consumed after the midpoint of eating.

Sleep Habit

The Munich Chronotype Questionnaire was employed to evaluate chronotype and sleep habits, which included sleep–wake timing, sleep duration, and circadian misalignment in sleep – social jetlag.[13] The Malay language validated version was employed in this study.[14]

Physical Activity

Physical activity levels were determined using the validated Malay version of the Global Physical Activity Questionnaire.[15]

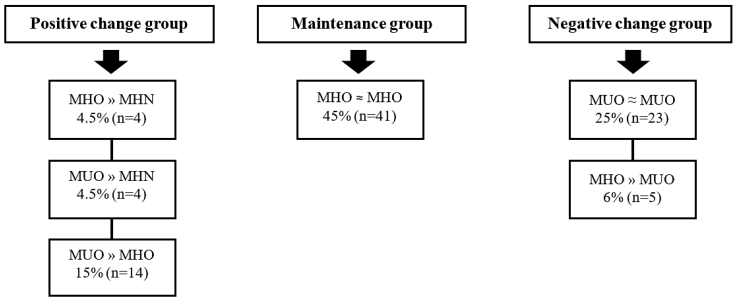

Fig.2 Transition in metabolic health phenotypes following weight reduction program. Abbreviation: MHO, metabolically healthy obesity; MHN, metabolically healthy normal weight; MUO; metabolically unhealthy obesity

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 29.0, with a significance level of $p \leq .05$. Histograms and computations of skewness and kurtosis were employed to evaluate normalcy. The Chi-square test was employed to examine categorical variables, while the Fisher exact test was used for dichotomous variables. For continuous variables related to socio-demographic data and participant attendance, a One-way ANOVA was conducted. One-way ANOVA was used to assess changes between metabolic health phenotype transition groups, with factors including adiposity, dietary intake, meal timing, temporal eating pattern, sleep habit and physical activity. The analysis was conducted using intention-to-treat data.

Results

Figure 2 shows the transition of metabolic health phenotypes following the weight reduction program. In the positive change group, there were 4 participants each from MHO and MUO transit to metabolically healthy normal weight (MHN). In addition, 14 participants improved from MUO to MHO. Meanwhile, 41 participants were classified

as MHO maintenance state whereby they are maintaining their MHO status. In the negative change group, 23 participants remained as MUO, and 5 participants transit from MHO to MUO.

Table 1 Sociodemographic characteristic and medical history of metabolic health phenotype groups

Parameter	Positive change (n=22)	Maintenance (n=41)	Negative change (n=28)	p-value
Gender [a]				
Men	6 (27)	7(17)	10(35)	0.210
Women	16 (73)	34 (83)	18(65)	
Age (years) [b]	40.3 ± 6.0	39.2 ± 7.2	39.5 ± 5.2	0.828
Marital Status [a]				
Single	2 (9)	12 (29)	5 (17)	0.153
Married	20 (91)	29 (71)	23 (83)	
Education level [a]				
Secondary	3 (13.6)	4 (9.8)	3 (10.7)	0.894
Tertiary	19 (86.4)	37 (90.2)	25 (89.3)	
Monthly household income [a]				
Low	2 (9)	7 (17)	1 (3)	0.558
Middle	16 (72)	24 (58)	21 (75)	
High	4 (19)	10 (25)	6 (22)	
Type 2 diabetes mellitus [a]				
Yes	1 (5)	0 (0)	5 (17)	**0.012**
No	21 (95)	41 (100)	23 (83)	
Hypertension [a]				
Yes	1 (5)	1 (2)	9 (32)	**<0.001**
No	21 (95)	40 (98)	19 (68)	
Hyper cholesterol [a]				
Yes	2 (9)	5 (12)	4(14)	0.855
No	20 (91)	36 (88)	24 (86)	
Smoking status [a]				
Yes	1 (5)	1 (2)	3 (11)	0.326
No	21 (95)	40 (98)	25 (89)	
Alcohol [a]				
Yes	0 (0)	0 (0)	0 (0)	N/A
No	22 (100)	41 (100)	28 (100)	
Chronotypes				
Morning type	16 (72.7)	20 (48.8)	10 (35.7)	**0.033**
Evening type	6 (27.3)	21 (51.2)	18 (64.3)	
Attendance to intervention [b]	10.6 ± 2.2	10.1 ± 2.3	8.9 ± 3.5	0.074

[a] Data are presented as number (%) using Chi-square test
[b] Data are presented as mean ± standard deviation using One-way ANOVA
[c] Data are presented as number (%) using Fisher exact test
Statistical significance is denoted by a bold p-value ($p<0.05$)

Table 1 shows that the majority of the participants were women, married, had tertiary education and came from middle-income groups. The negative change group had a higher prevalence of individuals with type 2 diabetes mellitus and hypertension compared to positive change and maintenance

groups. Interestingly, the positive change group had the greatest proportion of morning chronotype compared to the other groups. In terms of attendance to the weight reduction program, all three metabolic health transition groups had similar frequency.

Table 2 Factors associated with metabolic health phenotype transitions following weight reduction intervention

Parameter	Positive change (n=22)	Maintenance (n=41)	Negative change (n=28)	p-value
Adiposity				
Weight loss (kg)	-5.4 (-7.3, -3.6)	-3.9 (-5.3, 2.5)	-2.8 (-4.4, -1.2)	0.113
Weight loss (%)	-7.0 (-9.0, -5.0)[a]	-4.9 (-6.4, 3.3)	-3.2 (-5.0, -1.4)[a]	**0.022**
Fat loss (%)	-3.4 (-4.4, -2.3)[a]	-1.8 (-2.5, 1.0)	-1.3 (-2.2, -0.3)[a]	**0.013**
Fat free mass loss (kg)	-1.0 (-1.6, -0.5)	-1.0 (-1.4, 0.6)	-0.8 (-1.3, -0.3)	0.744
Visceral fat loss	-1.3 (-1.7, -0.8) [a]	-0.8 (-1.1, -0.5)	-0.5 (-0.9, -0.1) [a]	**0.030**
Dietary intake				
Total energy intake (kcal/day)	-531 (-709, -354)	-487 (-617, -357)	-401 (-558, -243)	0.525
Total CHO (%)	+0.5 (-2.3, 3.4)	-0.2 (-2.3, 1.9)	+2.2 (-0.3, 4.8)	0.348
Total protein (%)	+5.2 (3.3, 7.0)[a]	+3.8 (2.4, 5.1)[b]	+1.1 (-0.5, 2.8)[a b]	**0.004**
Total fat (%)	-5.5 (-8.5, -2.6)	-3.4 (-5.6, -1.2)	-3.3 (-5.9, -0.7)	0.448
Meal timing				
First mealtime (min)	-11.7 (-25.7, 2.2)	-2.6 (-12.8, 7.7)	-2.7 (-15.1, 9.7)	0.532
Last mealtime (min)	6.1 (-32.5, 44.8)	-27.4 (-55.8, 0.9)	-19.8 (-54.1, 14.5)	0.376
Midpoint of eating timing (min)	-2.1 (-22.3, 18.0)	-15.1 (-29.8, -0.3)	-12.2 (-30.1, 5.6)	0.584
Total eating duration (min)	17.9 (-24.3, 60.0)	-24.9 (-55.7, 6.0)	-17.1 (-54.5, 20.2)	0.259
Temporal eating pattern - Early eating window				
% Total E	+2.9 (-2.0, 7.8)	+2.6 (-1.0, 6.1)	+2.7 (-1.7, 7.0)	0.994
% E CHO	+1.6 (-1.7, 5.0)	+2.1 (-0.3, 4.7)	+3.9 (1.0, 6.9)	0.535
% E protein	+4.3 (2.5, 6.1) [a]	+2.6 (1.3, 3.8)	+1.1 (-0.5, 2.7) [a]	**0.029**
% E fat	-3.0 (-5.5, -0.4)	-2.4 (-4.3, -0.5)	-2.5 (-4.7, -0.2)	0.933
Temporal eating pattern - Late eating window				
% Total E	-2.9 (-7.8, 2.0)	-2.6 (-6.1, 1.0)	-2.7 (1.7, 7.0)	0.994
% E CHO	-1.1 (-3.9, 1.7)	-2.3 (-4.4, -0.3)	-2.2 (-4.7, 0.3)	0.766
% E protein	+0.9 (-0.2, 2.0)	+1.2 (0.4, 2.0)	+0.04 (-0.9, 1.0)	0.183
% E fat	-2.6 (-5.1, 0.1)	-1.0 (-2.9, 0.9)	-0.8 (-3.1, 1.5)	0.557
Sleep habit				
Sleep onset (hour)	-0.2 (-0.5, 0.2)	-0.1 (-0.4, 0.1)	-0.3 (-0.7, -0.01)	0.630
Sleep offset (hour)	-0.03 (-0.3, 0.2)	-0.05 (-0.2, 0.1)	-0.1 (-0.3, 0.1)	0.880
Sleep duration (hour)	+0.1 (-0.3, 0.6)	+0.1 (-0.2, 0.4)	+0.2 (-0.1, 0.7)	0.778
Social jetlag (min)	-4.0 (-18.4, 10.5)	-16.8 (-27.4, -6.2)	+0.6 (-12.1, 13.5)	0.095
Physical activity (MET)	+2423.6 (1332.5, 3514.7)	+1855.0 (1045.8, 2664.2)	+909.9 (-57.3, 1877.0)	0.110

Data are shown as changes in mean ± 95% confidence interval. Statistical significance is denoted by a bold p-value using One-way ANOVA. Abbreviations: CHO, carbohydrate; % E, percentage energy; NES, night eating score; Min, minute. a = significant differences between positive and negative change groups b = significant differences between maintenance and negative change groups

Table 2 presents the potential factors related to the transitions in metabolic health phenotypes following the weight reduction intervention. For adiposity parameters, the positive change group had the

greatest reduction in weight loss % (-7.0 ± 6.6 vs -3.2 ± 3.9, p=0.022), body fat % (-3.4 ± 3.7 vs -1.3 ± 2.1, p=0.013) and visceral fat loss (-1.3 ± 1.5 vs -0.5 ± 0.8, p=0.030) compared to the negative change group following the weight reduction intervention.

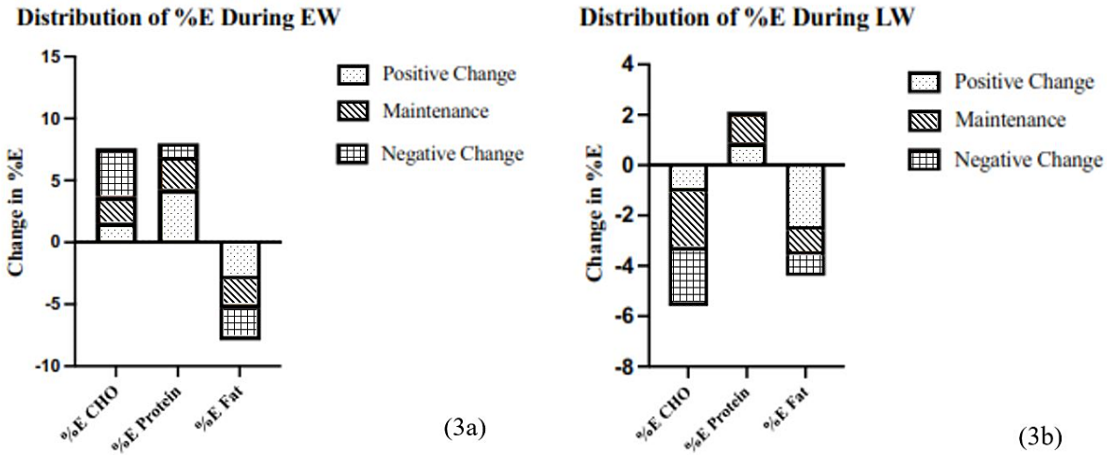

Fig. 3 (a) and (b) illustrate the change in percent E derived from each macronutrient during the early and late window. Abbreviation: %E, percent energy intake; EW, early window; LW, late window

For total dietary intake, all metabolic health phenotype groups experienced a similar trend in the reduction in overall caloric intake, carbohydrate, and fat consumption following the weight reduction intervention. However, the positive change group had the highest increment in total protein intake compared to the maintenance and negative change groups (p=0.004). Consequently, based on the temporal eating pattern, positive change groups had greatest increase in energy intake from protein during the early eating window compared to the remaining groups. Post hoc analysis shows that the positive change group had the greatest increase in energy intake from protein during early eating window compared to negative change group (+4.3 ± 3.8 vs +1.1 ± 4.9, p=0.024). The distribution of percent energy intake was also illustrated in Figure 3(a) and (b).

Following the weight reduction intervention, there were no differences between the metabolic health phenotype groups in meal timing, sleep habits and physical activity.

Discussion

This study demonstrated the transition of metabolic health phenotypes following a weight reduction intervention among adults with obesity, specifically between MHO, MUO and MHN individuals. This study highlighted the potential role of body weight and fat loss, protein intake and its temporal pattern as distinguishing factors between these metabolic health phenotype groups. Additionally, chronotypes could be another essential factor to be considered. The positive change group demonstrated a significant increase in protein intake as compared to the maintenance and negative change groups following the weight reduction program. A high-protein diet promotes feelings of fullness and aids in regulating appetite hormones. Research has shown that high-protein diets can acutely suppress appetite and promote fat mass loss while preserving lean mass.[16] A randomized controlled trial reported that the group of participants who were fed a diet rich in protein had significantly reduced body weight, BMI, waist circumference and metabolic markers, including insulin resistance, inflammatory marker and systolic blood pressure compared to the participants receiving low protein diet.[17] A high-protein diet reduces the production of the hunger hormone ghrelin and increases the production of the satiety-promoting peptide YY hormone, which can reduce the incidence of snacking, particularly on high-energy foods such as those from fat.[18]

In addition, our study showed that the positive change group had a greater increase in protein intake earlier in the day than the negative change group. Thus, greater protein intake during the early part of the day could be beneficial for metabolic health. Emerging studies are demonstrating that consuming a higher protein intake at the beginning of the day can possibly help regulate satiety and control appetite, preventing overfeeding later in the day.[19,20] A previous study had shown that an isoenergetic breakfast with egg had a significant increase in subjective satiety as well as satiety, hormone peptide YY and GLP-1 compared to an isoenergetic breakfast with steamed bread.[19] Supporting this finding, an updated meta-analysis of randomized controlled trials concluded that consumption of protein-rich breakfast could reduce subsequent energy consumption and thus aid in weight reduction.[21] Another possible mechanism of high protein breakfast in weight reduction and metabolic health could be linked to the sparing fat-free mass effect.[22,23] Prior research indicated that mice consuming a branched-chain amino acid (BCAA)-enriched diet in the early active phase (breakfast) exhibited superior skeletal muscle hypertrophy than those given a BCAA-supplemented diet in the late active phase (dinner), highlighting the potential impact of protein intake timing on muscle growth.[22] This underscores the need for studies that explore not only the quantity of protein intake but also the timing of its consumption.

The buildup of significant volumes of visceral adipose tissue is a key factor contributing to the elevated risk of cardiometabolic illness linked to abdominal obesity.[24] Obesity was linked with low-grade chronic inflammatory state, which was triggered from homeostatic stress due to continuous positive energy balance state.[25] In respond to positive energy balance, adipocytes increase in size (hypertrophy) and number (hyperplasia) to allow more lipid storage which would also result in increase in cytokine secretion, oxygen depletion, necrosis, activation of immune cells, and lead to further inflammatory response.[25] The current study findings emphasize the importance of reduction in body weight and adiposity to improve metabolic health whereby, the positive change group had demonstrated the highest weight reduction, especially reduction in body fat and visceral fat. Align with a previous study, obese adults with metabolic syndrome had higher visceral fat and at the same time had higher inflammation markers than those without metabolic syndrome.[8]

Furthermore, a prospective study demonstrated that the transition of MHO to MUO over 10 years was independently associated with accumulation in visceral fat area.[26] Since MHO is a transient state, intervention is necessary to prevent its progression to the MUO state, targeting visceral fat as a potential strategy.

Interestingly, our study showed that the positive change group had a greater proportion of morning chronotypes, while the negative change group had a greater proportion of evening chronotypes. Evening chronotypes have been associated with having higher BMI, insulin resistance and elevated plasma ghrelin levels than morning chronotypes.[27] Moreover, evening chronotypes tend to consume more unhealthy foods and engage in behaviours that could hinder weight reduction.[28] In contrast, morning chronotypes are more likely to adopt circadian rhythm-friendly eating patterns, with greater energy intake earlier in the day compared to evening chronotypes.[29] Therefore, future intervention studies should consider individual chronotypes as potential confounding factors that could significantly influence metabolic health transitions.

The results of the weight reduction program revealed a clear distinction between pre- and post-intervention physical activity levels, with all metabolic health transition groups showing increased physical activity level. However, no notable variations in physical activity were observed between the groups. This finding aligns with a study indicating that the interventions delivered were effective in increasing participation in physical activity. Moreover, even participants who engaged in less than 150 minutes per week experienced a decrease in the likelihood of metabolic syndrome.[30] The present investigation did identify any significant relationship between sleep duration and sleep circadian misalignment – specifically social jet lag with the transition of metabolic health phenotype groups among overweight/obese non-shift workers. Individual differences in sleep patterns and dietary habits may have played a role in the absence of an observed association.

Conclusion

In conclusion, this current research reveals that high protein intake, particularly during the early part of the day, weight reduction – especially in body fat and visceral fat – and chronotypes are significant factors associated with transitional changes in metabolic health phenotypes. These findings highlight the significance of meal timing and macronutrient distribution in dietary strategies for managing obesity. By integrating high protein intake into morning meals, healthcare professionals and dietitians can promote better metabolic health outcomes

However, the specific mechanisms by which these factors influence metabolic health remain unclear. Given the small and predominantly women sample size, these findings should not be generalized to the entire overweight or obese population. Further research is required to investigate other contributing factors and their effects on the transition of metabolic health phenotypes.

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Conflict of Interest

The author(s) declares no conflict of interest.

Data Availability Statement

Raw data of the findings in this study are available from the corresponding author.

Ethics Statement

This study received ethical approval from Ethical Committee of Medical Research of Universiti Kebangsaan Malaysia (UKM PPI/111/8/JEP- 2017-656).

Informed Consent Statement

Informed consent was obtained from study participants.

Clinical Trial Registration

This research does not involve any clinical trials.

Author Contributions

All authors provided substantial contribution to the study and approved the final manuscript:

- **Fatin Hanani Mazri:** Conceptualization, Project Administration, Methodology, Supervision, Writing – Final Draft.
- **Zahara Abdul Manaf:** Resources, Methodology, Supervision, Writing – Review.
- **Ti Mei Jun:** Analysis and Interpretation Results, Writing – Draft
- **Anas Ahmed Abdullah Al-Maswary:** Analysis and Interpretation Results, Writing – Draft
- **Divaashni Kannan:** Analysis and Interpretation Results, Writing – Draft
- **Nurul Hazimah Abdul Latif:** Analysis and Interpretation Results, Writing – Draft
- **Josefina Ramachandran:** Analysis and Interpretation Results, Writing – Draft
- **Fatin Umairah Mohd Keri:** Analysis and Interpretation Results, Writing – Draft
- **Maram Besaiso:** Analysis and Interpretation Results, Writing – Draft

References

1. Motwani M.S., Deorukhkar K.V., Sanwalka N., Kochrekar N.S., Pai A., Mitra A.M.S. Dietary Macronutrient and Micronutrient Intake Among Corporate Employees Aged 30 to 40 Years Residing in Mumbai, India. *Nutr Food Sci.* 2024;12(2). DOI:http://dx.doi.org/10.12944/CRNFSJ.12.2.18
2. Phillips C.M., Dillon C., Harrington J.M., McCarthy V.J.C., Kearney P.M., Fitzgerald A.P., Perry I.J. Defining Metabolically Healthy Obesity: Role of Dietary and Lifestyle Factors. *PLoS One*. 2013;8(10):e76188. DOI:10.1371/journal.pone.0076188
3. Numao S., So R., Matsuo T., Nakagaichi M, Tanaka K. A Favorable Metabolic Profile In Metabolically Healthy Obesity is Associated

with Physical Activity Level Rather than Abdominal Fat Volume in Japanese Males. *J Phys Ther Sci.* 2021;33(2):137-141. DOI:10.1589/jpts.33.137

4. Chen Y., Ma L., Han Z., Xiong P. The Global Burden of Disease Attributable to High Body Mass Index in 204 Countries and Territories: Findings from 1990 to 2019 and predictions to 2035. Diabetes, *Obes Metab.* 2024;26(9):3998-4010. DOI:https://doi.org/10.1111/dom.157485.
5 Mazri F.H., Manaf Z.A., Shahar S., Mat Ludin A.F., Karim N.A., Hazwari N.D.D., Kek Q.W., Abdul Basir S.M., Arifin A. Do Temporal Eating Patterns Differ in Healthy versus Unhealthy Overweight/Obese Individuals? *Nutrients.* 2021;17;13(11):4121. DOI: 10.3390/nu13114121.
6. Caleyachetty R., Thomas G.N., Toulis K.A., Mohammed N., Gokhale K.M., Balachandran K., Nirantharakumar K. Metabolically Healthy Obese and Incident Cardiovascular Disease Events Among 3.5 Million Men and Women. *J Am Coll Cardiol.* 2017;70(12):1429-1437. DOI:10.1016/j.jacc.2017.07.763
7. Hamzeh B., Pasdar Y., Moradi S., Darbandi M., Rahmani N., Shakiba E., Najafi F. Metabolically Healthy Versus Unhealthy Obese Phenotypes in Relation to Hypertension Incidence; A Prospective Cohort Study. *BMC Cardiovasc Disord.* 2022;22(1):106. DOI:10.1186/s12872-022-02553-5
8. Koster A., Stenholm S., Alley D.E., Kim L.J., Simonsick E.M., Kanaya A.M., Visser M., Houston D.K., Nicklas B.J., Tylavsky F.A., Satterfield S., Goodpaster B.H., Ferrucci L., Harris T.B. Body Fat Distribution and Inflammation Among Obese Older Adults With and Without Metabolic Syndrome. *Obesity (Silver Spring).* 2010;18(12):2354-2361. DOI:10.1038/oby.2010.86
9. Mazri F.H., Manaf Z.A., Shahar S., Mat Ludin A.F., Abdul Basir S.M. Development and Evaluation of Integrated Chrono-Nutrition Weight Reduction Program among Overweight/Obese with Morning and Evening Chronotypes. *Int J Environ Res Public Health.* 2022;19(8):4469. DOI:10.3390/ijerph19084469
10. Alberti K.G.M.M., Eckel R.H., Grundy S.M., Zimmet P.Z., Cleeman J.I., Donato K.A., Fruchart J.C., James W.P., Loria C.M., Smith S.C.J. Harmonizing the metabolic syndrome: A Joint Interim Statement of The International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World heart federation; International . *Circulation.* 2009. DOI:10.1161/CIRCULATIONAHA.109.192644
11. Hosseinpanah F., Tasdighi E., Barzin M., Mahdavi M., Ghanbarian A., Valizadeh M., Azizi F. The Association between Transition from Metabolically Healthy Obesity to Metabolic Syndrome, and Incidence of Cardiovascular Disease: Tehran Lipid and Glucose Study. *PLoS One*. 2020. DOI:10.1371/journal.pone.0239164
12. Shahar S., Earland J., Rahman S.A. Validation of A Dietary History Questionnaire Against A 7-D Weighed Record for Estimating Nutrient Intake Among Rural Elderly Malays. *Malays J Nutr.* 2000;6(1):33-44. PMID: 22692390
13. Roenneberg T., Wirz-Justice A., Merrow M. Life between clocks: Daily Temporal Patterns of Human Chronotypes. *J Biol Rhythms.* 2003;18(1):80-90. DOI:10.1177/0748730402239679
14. Mazri F.H., Manaf Z.A., Shahar S, Mat Ludin A.F., Karim N.A., Ban A.Y., Osman R.A. Modified Munich Chronotype Questionnaire for Application to Short-Interval Split Sleep of Non-Shift Workers. *Chronobiol Int.* 2021;38(5):659-665. DOI:10.1080/07420528.2021.1887209
15. Soo K.L., Wan Abdul Manan W.M., Wan Suriati W.N. The Bahasa Melayu version of the Global Physical Activity Questionnaire: Reliability and Validity Study in Malaysia. *Asia-Pacific J Public Heal.* 2015;27(2):184-193. DOI:10.1177/1010539511433462
16. Morrison C.D., Laeger T. Protein-Dependent Regulation of Feeding and Metabolism. Trends Endocrinol Metab. 2015;26(5):256-262. DOI:10.1016/j.tem.2015.02.008
17. Yılmaz S.K., Eskici G., Mertoğlu C., Ayaz A. Effect of Different Protein Diets on Weight Loss, Inflammatory Markers, and Cardiometabolic Risk Factors in Obese Women. *J Res Med Sci.* 2021;26(1). DOI: 10.4103/jrms.JRMS_611_20

18. Leidy H.J., Armstrong C.L.H., Tang M., Mattes R.D., Campbell W.W. The Influence of Higher Protein Intake and Greater Eating Frequency on Appetite Control in Overweight and Obese Men. *Obesity (Silver Spring).* 2010;18(9):1725-1732. DOI:10.1038/oby.2010.45
19. Wang S., Yang L., Lu J., Mu Y. High-Protein Breakfast Promotes Weight Loss By Suppressing Subsequent Food Intake and Regulating Appetite Hormones in Obese Chinese Adolescents. *Horm Res Paediatr.* 2015;83(1):19-25. DOI:10.1159/000362168
20. Park Y.M., Heden T.D., Liu Y., Nyhoff L.M., Thyfault J.P., Leidy H.J., Kanaley J.A. A High-Protein Breakfast Induces Greater Insulin and Glucose-Dependent Insulinotropic Peptide Responses to a Subsequent Lunch Meal in Individuals with Type 2 Diabetes. *J Nutr.* 2015;145(3):452-458. DOI:https://doi.org/10.3945/jn.114.202549
21. Qiu M., Zhang Y., Long Z., He Y. Effect of Protein-Rich Breakfast on Subsequent Energy Intake and Subjective Appetite in Children and Adolescents: Systematic Review and Meta–Analysis of Randomized Controlled Trials. *Nutrients.* 2021;13(8). DOI:10.3390/nu13082840
22. Aoyama S., Kim H.K., Hirooka R., Tanaka M., Shimoda T., Chijiki H., Kojima S., Sasaki K., Takahashi K., Makino S., Takizawa M., Takahashi M., Tahara Y., Shimba S., Shinohara K., Shibata S. Distribution of Dietary Protein Intake in Daily Meals Influences Skeletal Muscle Hypertrophy via the Muscle Clock. *Cell Rep.* 2021;36(1). DOI:10.1016/j.celrep.2021.109336
23. Khaing I.K, Tahara Y., Chimed-Ochir O., Shibata S., Kubo T. Effect of Breakfast Protein Intake on Muscle Mass and Strength in Adults: A Scoping Review. *Nutr Rev. January* 2024:nuad167. DOI:10.1093/nutrit/nuad167
24. Elffers T.W., de Mutsert R., Lamb H.J., de Roos A., Willems van Dijk. K., Rosendaal F.R., Jukema J.W., Trompet S. Body Fat Distribution, in Particular Visceral Fat, is Associated with Cardiometabolic Risk Factors in Obese Women. *PLoS One.* 2017;12(9):e0185403. DOI:10.1371/journal.pone.0185403
25. Karczewski J., Śledzińska E., Baturo A., Jończyk I., Maleszko A., Samborski P., Begier-Krasińska B., Dobrowolska A. Obesity and Inflammation. *Eur Cytokine Netw.* 2018;29(3):83-94. DOI:10.1684/ecn.2018.0415
26. Hwang Y.C., Hayashi T., Fujimoto W.Y., Kahn S.E., Leonetti D.L., McNeely M.J., Boyko E.J. Visceral Abdominal Fat Accumulation Predicts the Conversion of Metabolically Healthy Obese Subjects to An Unhealthy Phenotype. *Int J Obes.* 2015;39(9):1365-1370. DOI:10.1038/ijo.2015.75
27. Ekiz Erim S., Sert H.. The Relationship Between Chronotype and Obesity: A Systematic Review. Chronobiol Int. 2023;40(4):529-541. DOI:10.1080/07420528.2023.2180385
28. Mazri F.H., Manaf Z.A., Shahar S, Mat Ludin A.F. The Association Between Chronotype and Dietary Pattern Among Adults: A Scoping Review. *Int J Environ Res Public Health.* 2020;17(1):68. DOI:10.3390/ijerph17010068
29. Xiao Q., Garaulet M., Scheer F.A.J.L. Meal timing and Obesity: Interactions with Macronutrient Intake and Chronotype. *Int J Obes.* 2019;43(9):1701-1711. DOI:10.1038/s41366-018-0284-x
30. Kettle V.E., Madigan C.D., Coombe A.,Graham H., Thomas J.J.C., Chalkley A.E. Effectiveness of Physical Activity Interventions Delivered or Prompted By Health Professionals in Primary Care Settings: Systematic Review and Meta-Analysis of Randomised Controlled Trials. *BMJ.* 2022;376. DOI:10.1136/bmj-2021-068465