Psychological Factors Influenced by Metabolic Health

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Abstract

Metabolic syndrome is a group of metabolic risk factors that include obesity, dyslipidemia, and insulin resistance. The purpose of this study was to monitor metabolic and psychological changes after following a strict clean ketogenic diet (CKD) of 20 grams of carbohydrates or an intermittent fasting diet with CKD (IF + CKD). The findings from this study demonstrate that adhering to a CKD over a 30-day period may result in improvements in metabolic health and psychological symptoms. Additionally, participants who use IF + CKD show even more improvement. Forty-seven participants completed a pre and post-test study with body measurements, lab work, and psychological testing. The findings revealed that after a duration of 30 days, both the fasting and the non-fasting groups exhibited improvements in lipid panel ratios, psychological symptoms, physical symptoms, and visceral fat reduction. However, these improvements were significantly greater in the IF + CKD group compared to the non-fasting group. Both groups experienced improvements in anxiety levels, daytime sleepiness, and energy levels, however, well-being only improved for the IF + CKD group.

Keywords

Metabolic Syndrome, Metabolic Health, Clean Ketogenic Diet, Intermittent Fasting

1. Introduction

Metabolic health serves as a crucial indicator of general well-being, as it reflects the efficient use of energy sources to support essential physiological processes.
However, recent studies raise concerns about the prevalence of metabolic disorders among adults in the United States. Araújo et al. (2018) analyzed data from the *National Health and Nutrition Examination Survey*, and they found that a staggering 88% of U.S. adults were classified as metabolically unhealthy. According to the WHO, metabolic syndrome includes health concerns, like hypertension, abdominal obesity, elevated blood sugar levels and abnormal cholesterol levels (WHO, 2022). O’Hearn et al. (2022), suggested that closer to 93% of U.S. adults were metabolically unhealthy. These findings underscore the urgent need to prioritize the study and improvement of metabolic health.

The argument that metabolic health is instrumental to overall health became apparent during the recent pandemic. Individuals with underlying cardiometabolic diseases, such as diabetes mellitus, obesity, hypertension, and heart failure experienced disproportionately higher rates of hospitalization due to COVID-19. Based on their research, O’Hearn et al. (2021) estimated that a significant number of COVID-19 hospitalizations in the United States were attributed to these cardiometabolic conditions and went on to suggest that a 10% reduction in each of these conditions could have potentially decreased hospitalizations by approximately 11%. This highlights the crucial role of metabolic health in determining disease outcomes and the importance of developing strategies to address and mitigate the impact of future pandemics.

Studying the possible underlying causes of metabolic syndrome is key to its reversal. Bikman (2020), highlights insulin resistance as a prevalent underlying factor in various metabolic diseases. Metabolic inefficiency and insulin resistance not only influence physiological health issues, but this combined effect has extensive consequences on mental health and the presence of psychological disorders. Extensive research has shed light on a compelling association between insulin resistance, metabolic syndrome, and psychiatric disorders, revealing a worrisome interplay that requires further study. Researchers discovered increased mental disorders, such as anxiety, depression and bipolar disorder linked with metabolic syndrome (Butnoriene et al., 2018; Bai et al., 2016; Penninx & Lange, 2018). More recently, Johnson et al. (2023) established the crucial role of insulin resistance in Alzheimer’s Dementia. These findings emphasize the crucial role of hyperinsulinemia, elevated levels of insulin, paired with insulin resistance in the development and consequences of metabolic syndrome on mental health and cognitive functioning.

Additionally, metabolic inefficiencies present a variety of physical and mental health issues. Sometimes the mental issues are overlooked or left untreated. According to Butnoriene et al. (2018) psychiatric conditions, like anxiety and depression, although prevalent in primary care settings, are often undiagnosed or overlooked. Also, it has been found that the use of certain medications, particularly mood stabilizers and second-generation antipsychotics, commonly prescribed for long-term mental illness, have been associated with an increased risk of developing metabolic syndrome (Penninx & Lange, 2018), so it is hard to
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know which health issue came first. While psychotropic medications may be beneficial for managing psychiatric symptoms, they do not address the root cause and have metabolic side effects. These findings emphasize why it is important to study these connections and determine the influence of metabolic disorders on mental illness.

Palmer (2019) likewise confirms this relationship between insulin resistance and metabolic disorders to be a strong factor in the presence and severity of psychiatric conditions. Palmer believes that when mitochondria fail to function properly, it can potentially lead to negative psychological consequences, a phenomenon he refers to as “low brain energy”. Furthermore, he directly ties this low metabolic energy state closely to poor nutrition, poor microbiome or gut health, and insulin resistance, hence making the case for research using nutritional interventions to help improve neurological issues like mental illness.

A Ketogenic Diet (KD) usually emphasizes consuming high-fat, low-carbohydrate foods with a moderate intake of protein. It is designed to shift metabolism into a state called ketosis, where the body uses the fat as energy instead of the glucose produced by carbohydrates (Johnson et al., 2020). During the transition from glucose to ketone fuel, individuals may experience changes in hunger, mood, and even temporary cognitive lapses until the body adapts to the dietary changes (de Cabo & Mattson, 2019). The KD has a long history of medical use and has gained renewed interest in recent years for its potential therapeutic effects on various metabolic health issues. It has been studied for conditions such as cancer, epilepsy, and diabetes (Freeman et al., 2023; Athinarayanan et al., 2020); seizures, autism spectrum disorders (Amari et al., 2015); hyperglycemia, obesity, and hypertriglyceridemia (Dyson, 2020; Tinguely et al., 2021).

More recently, a KD is being explored as a treatment option for psychiatric disorders (Palmer, 2019). According to Yu et al. (2023) and Hawkins et al. (2018) in this state of ketosis, the body effectively uses ketones as a preferred food source compared to using glucose. Furthermore, CKD is an elimination diet to help address gut health issues and autoimmune conditions (Le & Johnson, 2020; Martin, 2020) and typically involves a macronutrient diet breakdown of 70% fat, 20% protein, and 10% unprocessed carbohydrates. Additionally, some studies focus on limiting refined sugars, starches, seed oils, and high fructose corn syrup (HFCS), especially in liquid form, as this exacerbates the negative impact on the gut. According to Johnson et al. (2023), HFCS, unlike glucose, may trigger both maladaptive metabolic processes and insulin resistance, potentially leading to brain inflammation, elevated uric acid, and various mental health issues.

While KD studies show promising results, another dietary strategy that has emerged as a potential ally in promoting metabolic health is time restricted eating (TRE), also called intermittent fasting (IF). TRE involves reducing the window of time during which food is consumed over the day, compared to fasting or snacking throughout the day. Research shows that IF offers numerous benefits, including enhanced weight loss, especially visceral fat (Tinsley & LaBounty,
improvements in blood pressure and lipid panels (Ahmed et al., 2021); improved insulin sensitivity (Yuan et al., 2022); better glycemic control (Parr et al., 2023); and reduce inflammation and oxidative stress (Dong et al., 2020), independent of the specific types of foods consumed.

Findings from the previous studies support the importance of timed eating on glucose control and other metabolic factors (Patterson & Sears, 2017). Interestingly, there are overlapping mechanisms impacted by KD and TRE that contribute to their beneficial effects on metabolic health. Both approaches promote fat utilization for energy, improve insulin sensitivity, and reduce inflammation. Additionally, they influence gene expression and support the production of ketone bodies, which can further enhance metabolic health. These findings collectively suggest that IF can improve metabolic health and potentially contribute to longevity (Patterson et al., 2015).

Given that findings from several studies indicate positive changes in metabolic health from both 1) low carbohydrate diets, particularly those with reduced HFCS and ultra-processed foods, and 2) the restriction of food consumption to a smaller window, compared to a fasting window, the purpose of the current study was to examine the combined effect of these two strategies compared to the single strategy. Metabolic health was measured by a blood lipid panel, fat mass, as well as a survey of physical and psychological symptoms. By investigating the synergistic impact of these approaches, researchers aimed to gain insights into how metabolic function could be further enhanced through nutritional strategies.

Hypotheses

1) It was expected that both groups (CKD & IF + CKD) were expected to experience improvements across the metabolic risk factors, including, decreased fat mass and body fat percentage and reductions in triglycerides and an increase in HDL cholesterol. Also, both groups were expected to improve in different physical and psychological symptoms, including, mood, anxiety, reduced daytime sleepiness and inflammation byproducts, such as joint pain, body aches and rashes.

2) Improvements were expected to be more pronounced in individuals adhering to IF + CKD, compared to those who were following the CKD, as cited in past literature of the synergistic effects of this combined dietary change.

2. Method

2.1. Participants

Participants were recruited for this 30-day study through university wide e-mails and local community flyers. Initially, 66 participants were recruited, but only 47 completed the full 30-day protocol and submitted completed dietary logs. Several individuals dropped out of the study citing reasons such as preference for food variety or feeling unwell with low energy on the diet. The reduced energy and fogginess align with the metabolic energy shift as described by de Cabo & Mat-
The final data set consisted of 15 males and 32 females who were randomly assigned to either follow a CKD + IF group \( (n = 25) \), with an 8-hour restrictive feeding window (mean age = 40.76; SD = 12.35), or a CKD group \( (n = 22) \) without specific feeding time restrictions. Participants were guaranteed confidentiality and had the freedom to decline or withdraw from the study at any time.

The study received certification as an Expedited Review by the Institutional Review Board. Number: 2021-872-E05-4065/MacK, Ang. The study was funded by the University of Tennessee at Martin Faculty Development Program.

2.2. Materials and Procedure

2.2.1. Materials

**Epworth Sleepiness Scale (ESS; Johns, 1991):** The ESS measures general daytime sleepiness by assessing the likelihood of falling asleep in eight different scenarios. Each question is rated from 0 (no chance of dozing) to 3 (high chance of dozing). The total score on the scale ranges from 0-24, with higher scores indicating greater daytime sleepiness. The ESS has been widely used and validated as a reliable measure of daytime sleepiness.

**Stress Profile Inventory (SPI; Nowack, 1999):** The SPI is a comprehensive instrument that measures 15 subscales related to stress and health risk. For the current study, the subscales of health habits and psychological well-being were utilized. The SPI has demonstrated good reliability and validity in assessing stress-related factors.

**Nutritional Efficacy Scale (NES; Schwarzer & Renner, 2000):** The NES is a subscale of a larger health-specific self-efficacy scale. It measures an individual’s belief in their ability to succeed in making nutritional changes. The score on the NES were compared between participants who dropped out of this study and those who completed it, providing insights into the impact of mindset on dietary changes. The NES has shown good reliability and validity in previous research.

**Medical History Questionnaire:** A general medical survey was administered to collect information on participants personal medical history, current medication use, and family history of medical diagnosis. The questionnaire helped assess potential confounding factors and allowed for a comprehensive understanding of participants health backgrounds.

**Pre-test General Information Survey:** this survey assessed participants general patterns of behavior, food and dietary intake, probiotic use, antibiotic use, gestational diabetes history (if applicable), and nicotine product usage. It provided important baseline data for the study and contributed to a comprehensive understanding of participants behaviors and characteristics.

**Daily Log Sheets:** participants were provided with daily log sheets to record their food and fluid intake, mealtimes, and their subjective feelings before and after eating. These log sheets served as a measure of accountability for food choices and may have provided insight into any psychological or physical changes experienced after consuming specific foods. They also increased the
participants’ mindfulness of their food choices, which may have influenced the study outcomes.

*BOD POD®* (Cosmed): The BOD POD® is a body composition measurement device that uses air displacement plethysmography (ADP) to assess fat mass compared to fat free mass standard procedures for measuring height, weight, thoracic gas volume, and air displacement were followed inside the bipod chamber. Participants wore appropriate attire (e.g., swimming cap, bathing suit, or spandex outfit and parentheses for the measurement, and their weight was calibrated before testing. The BOD POD® has been extensively validated and is considered a reliable tool for body composition analysis.

*ACSM’s guidelines for exercise testing and prescription* (American College of Sports Medicine, 2000): The standardized procedures recommended by a CSM were employed for height, weight, hand grip, and skinfold measurements. These measurements were used to assess participants physical characteristics and fitness levels.

*CardioChek® Plus Professional* (PTS Diagnostics): This device was used to measure triglycerides and HDL. The ratio of triglycerides to HDL is indicative of both a healthy diet and aerobic exercise (Wakabayashi & Daimon, 2019). A lower ratio is generally preferred, as it suggests larger cholesterol particles that support healthier blood vessels (Bikman, 2020). Higher ratios, on the other hand, may indicate greater metabolic health risks. The CardioChek® plus professional device has been validated and is widely used for assessing the lipid profile in both research and clinical settings.

### 2.2.2. Procedure

#### Pretest

Participants attended an initial baseline data collection and information session, approximately two weeks before the testing phase was to begin. In addition to collecting baseline data, this information session gave participants the necessary information to provide to their doctors about any health concerns before participating. As well, participants were given a list of acceptable low carbohydrate foods (Berg, 2022) and the standard instructions to gradually decrease the consumption of refined sugars, HFCS, and seed oil intake to minimize possible dietary shocks to their systems during the testing phase.

Baseline body measurements were collected during this session, including height, weight, waist, arm, and leg circumference, as well as grip strength. Grip strength has been used as an indirect measure of inflammation. A blood draw was performed to measure HDL cholesterol and triglycerides. Fat mass and body fat percentages were assessed using the BOD POD® chamber or caliper measurements if a participant expressed discomfort in the confined space of the BOD POD®.

Participants were assigned to either the CKD or the CKD + IF using a randomized control trial design. Both groups were instructed to adhere to a CKD, which involved avoiding processed foods, including packaged “keto friendly”
options, and limiting carbohydrate intake to no more than 20 grams per day from the approved food list. In addition to following the restricted carbohydrate intake the CKD + IF group was asked to restrict eating to an 8-hour feeding window and maintain a 16-hour fasting. This design allowed for a comparison between the effects of the CKD to the CKD + IF. Random assignment of participants of the groups helped minimize bias and ensure that they observed differences that could be attributed to the interventions rather than individual characteristics and desires.

Before the 30-day testing phase commenced, participants were asked to complete a baseline survey through an online Qualtrics link. The survey gathered pretest survey data and relevant information about the participants demographics, behaviors, and pretest health status. Nutritional efficacy data were collected at baseline only.

To provide ongoing support, participants were assigned a designated contact person who communicated with them once a week, usually Sunday evening, via e-mail or text messages. The support person sent weekly reminders and was available to address any questions or concerns that arose during the study. Participants were able to choose their preferred method of communication as a way of decreasing the number of participant dropouts during this study.

Post-test

At the conclusion of the 30-day period, participants were invited to attend a posttest session, which replicated the measurements taken during the pretest. During this session participants were asked to submit their completed daily log sheets, which documented their food and fluid intake, mealtimes, and subjective feelings before and after eating. This allowed for a comprehensive analysis of participant adherence to the prescribed diet and potential changes in dietary behaviors.

Additionally, participants attended a debriefing session and were provided with detailed explanations of the study's purpose, procedures, and any relevant finding or implications. This debriefing was to ensure that participants understood the goals of the study and to address any questions or concerns. At the end of the posttest session, participants were given the option to either continue with this study for an additional three weeks or conclude participation after the initial 30-day period. By offering participants the choice to continue or end their involvement in the intervention, researchers gained insight into participant perception of the intervention’s effectiveness, acceptability, and feasibility. Additionally, it provided the opportunity to observe any potential differences in outcomes between those who opted for continued participation and those who chose to discontinue.

Participants were informed that the dietary modifications may have had an impact on their gut microbiome and were advised to reintroduce foods not consumed within the last 30 days gradually. This recommendation was intended to help participants transition back to their regular eating patterns if de-
sired, while minimizing any potential discomfort or disruptions to their digestive system.

3. Results

3.1. Statistical Analysis

A series of paired samples t-tests were conducted separately for the CKD and CKD + IF groups to examine the metabolic changes between baseline and final values. Parametric tests were utilized because assumptions of normality and homogeneity of variance were satisfied.

3.2. Lipid Panel

Both groups demonstrated improvements, however, the CKD + IF exhibited a significant decrease in the TG/HDL ratio, indicating a notable improvement from a baseline value of 3.58 to 2.60. On the other hand, the CKD group showed improvement in the ratio, but the change was not significant, as it moved from a 3.87 at baseline to a 3.60 at post-test. When examining the triglyceride values, a significant decrease was observed in the CKD + IF group, while the CKD group did not show a significant change, although it did decrease. Both groups also displayed significant reductions in HDL values also decreased significantly in both groups (See Table 1).

3.3. Body Measurements and Grip Strength

Both the CKD + IF and CKD groups exhibited significant weight loss in pounds. Additionally, both groups demonstrated significant reductions in fat mass, waist circumference, and hip circumference. Grip strength improved in the CKD + IF group, specifically in the right hand (See Table 1).

3.4. Psychological

Both groups experienced decreases in anxiety levels and reported energy levels improved. Feelings of well-being only improved for CKD + IF (See Table 1).

3.5. Physical

Significant improvements were found in both group in joint pain, a common outcome of inflammation, however, rashes only improved in the CKD group (See Table 1).

4. Discussion

The current understanding of the effects of CKD + IF on metabolic health and psychological well-being was explored in this study. The findings revealed that after a duration of 30 days, both the fasting and the non-fasting group exhibited improvements in lipid panel ratios, psychological symptoms, physical symptoms, and body fat composition. However, these improvements were significantly greater in the CKD + IF group compared to the non-fasting group.
Table 1. Average pre-and post-study lipid panel (Triglycerides, HDL, Triglyceride/HDL ratio), body measurements (waist, hips, body fat %, fat mass, grip strength) and mental factors (sleepiness, well-being, health habits, anxiety, energy) and physical symptoms (joint pain, rashes, aches) separately by CKD + IF (n = 25) and CKD (n = 22) group.

<table>
<thead>
<tr>
<th>CKD + IF</th>
<th>Pretest</th>
<th>Posttest</th>
<th>(n = 25)</th>
<th>M</th>
<th>SD</th>
<th>M</th>
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<tr>
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<td>44.01</td>
<td>192.39</td>
<td>39.64</td>
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<tr>
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<tr>
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<td>5.28</td>
<td>43.00</td>
<td>4.72</td>
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<td>30.56</td>
<td>9.69</td>
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<td>&lt;0.001</td>
<td>1.19</td>
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<td>0.212</td>
<td>0.178</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grip strength (left)</td>
<td>31.61</td>
<td>10.31</td>
<td>31.02</td>
<td>9.39</td>
<td>0.775</td>
<td>0.224</td>
<td>0.169</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
4.1. Psychological Health Improvements

The significant health improvements observed in the CKD + IF group could be attributed to several potential mechanisms. It was hypothesized that IF may enhance key metabolic processes, such as autophagy, or the removal of dysfunctional cells (Vasim et al., 2022), improved insulin resistance (Bikman, 2020), and modulating gut microbiome (Le & Johnson, 2020; Martin, 2020; Jain & Li, 2023), or a combination of these factors (Long & Panda, 2022; Vasim et al., 2022). These factors coupled with lower insulin levels, that come with the reduction of processed carbohydrates, may explain the greater improvements observed in psychological and cognitive functioning, as well as physical symptoms. Previous studies demonstrate a strong association between poor metabolic health in psychological conditions, such as depression, anxiety (Butnoriene et al., 2018) and bipolar disorders (Bai et al., 2016). Intermittent fasting appears to offer potential enhanced benefits for mental health issues, along with decreased processed carbohydrate intake. The study demonstrated a significant improvement in anxiety levels. The participants reported improved energy levels and decreased daytime sleepiness. The importance of intermittent fasting with a clean ketogenic diet was evident as well-being improved in the group that followed the CKD + IF.

4.2. Physical Health Improvements

The triglyceride/HDL ratio, a key marker of cardiovascular risk, showed more notable improvements in the CKD + IF group compared to the CKD. Only this group experienced a significant shift towards the desired low risk ratio of 2.0 whereas the non-fasting group remained within the borderline high range (Wakabayashi & Daimon, 2019; Bikman, 2020). Although both groups demonstrated
decreased triglyceride values, the CKD + IF group successfully moved from the borderline high range (150 to 199 mg/dL) to the normal range (less than 150 mg/dL), whereas the CKD, non-fasting group showed improved numbers, but they stayed within the borderline high range. Both groups experienced a slight decrease in HDL, often referred to as good cholesterol, which may occur during short-term dietary and physical activity changes (Wakabayashi & Daimon, 2019), but the numbers remained within the normal range and did not reach the high-risk range for cardiovascular risk.

4.3. Limitations & Future Research

It is essential to acknowledge the limitations regarding the relatively short duration of this study, which was only 30 days. While this time frame allowed for the observation of improvements in lipid panel numbers, it may not fully capture the long-term effects of the intervention (Dong et al., 2020). Metabolic changes, particularly those related to lipid profiles can take time to manifest and stabilize. Long term effects of dietary interventions, such as very low carbohydrate diets and intermittent fasting may differ from short-term effects. Longer durations would enable researchers to assess the sustainability of the observed improvements and potentially uncover additional effects that may not be apparent within a shorter time frame. Moreover, metabolic health and its association with various health outcomes, including cardiovascular risk can be influenced by multiple factors and may require extended periods of intervention to observe substantial and lasting effects.

In addition to self-report measures, dietary studies often face challenges in accurately assessing participants' adherence to prescribed diets. Participants may deviate from the recommended dietary guidelines, consume unreported food items, or fail to accurately record food intake. These discrepancies between actual dietary behaviors and reported intake can impact the validity of the results and introduce uncertainty in interpreting the findings. Therefore, it is crucial to consider these limitations while interpreting the outcomes of dietary studies and to explore alternative methods, such as objective dietary assessments, to improve the accuracy of data collection.

While the present study made efforts to mitigate the limitations of a diet study by providing participants with clear dietary guidelines and monitoring adherence, the potential for discrepancies between reported and actual dietary intake remains a concern. Future studies could consider employing more objective methods, such as dietary biomarkers or digital detailed food diaries, to obtain a more accurate and reliable assessment of participants dietary adherence.

4.4. Conclusion

In conclusion, the findings from this study demonstrate that adhering to a CKD diet over a 30-day period may result in improvements in metabolic health, psychological symptoms, and physical well-being. Moreover, the inclusion of IF
appears to augment these benefits further. However, it is crucial to acknowledge that further clinical research is warranted to explore the efficacy of both short-term and long-term interventions across specific psychiatric disorders and diverse demographic groups. Longitudinal studies with larger sample sizes are necessary to establish the generalizability and statistical power of the findings. The duration of interventions should be extended to assess long-term effects and sustainability of the observed improvements. Continued scientific inquiry will contribute to advancing our knowledge in this area and inform evidence-based practices for promoting metabolic health and psychological well-being.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References


