The role of chrononutrition in weight loss
El papel de la crononutrición en la pérdida de peso

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ABSTRACT

Keywords: number of meals, frequency, schedule and intermittent fasting

Circadian clocks and nutrition are closely related. The number of meals, the timing of consumption, and other factors can influence a person's weight and metabolism. The aim of this study is to gather scientific evidence that supports the idea that circadian rhythms affect weight loss. This is a bibliographic review that utilizes 56 references, with Pubmed being the most frequently used database, followed by Google Academic. The review discussion is divided into three categories: meal frequency, meal schedule, and intermittent fasting. Most studies agree that a greater intake of food should be consumed in the morning, but it's essential to note that the type of meals consumed during this time is also crucial for weight loss. Regarding the number of meals, there is more disagreement, so more research is needed. Finally, intermittent fasting appears to be effective for certain groups of people. After conducting a thorough study, we have concluded that there is a correlation between circadian cycles and body weight. However, further research with appropriate clinical studies is needed. It is advisable to consult a professional before making any sudden changes to your diet.

RESUMEN

Palabras clave: número de comidas, frecuencia de comidas, horario y ayuno intermitente

Los relojes circadianos están muy relacionados con la nutrición. La cantidad de comidas, el horario en el que se realizan y otros parámetros parece ser que puede influir en el peso y metabolismo de una persona. El objetivo de este estudio es recopilar evidencia científica de que los ritmos circadianos tienen influencia en la pérdida de peso. Se trata de una revisión bibliográfica. Se utilizaron 56 referencias. Siendo Pubmed la base de datos más utilizada seguido de Google académico. La discusión de los estudios encontrados se ha separado en: frecuencia de comidas, horario de comidas y ayuno intermitente. Con respecto al horario de las comidas, la mayor parte de los estudios coinciden en una mayor ingesta durante la mañana. Respecto al número de comidas hay mayor controversia por lo que tiene que haber mayor investigación. Por último, el ayuno intermitente, depende que grupo de personas parece funcionar muy bien. Tras haber hecho un profundo estudio, se llega a la
Introduction

Chrononutrition is a very controversial topic today. Chrononutrition is a concept directly related to metabolism, pancreatic function and hormone secretion (1). The timing of meals, the number and sequence of meals play a very important role at a physiological and hormonal level.

Recent research suggests that metabolic processes exhibit circadian rhythmicity (2). What are circadian rhythms? These are the physical, mental and behavioral changes that follow a 24-hour cycle. These natural processes respond mainly to light and darkness and affect most living things.

Circadian rhythms can be affected by: hormone release, temperature regulation, and regulation of eating habits and digestion. A very important aspect is the role of circadian rhythms in sleep patterns. This is regulated by the suprachiasmatic nucleus (SCN), which is said to be the central nucleus (3).

The chronotype is distinguished according to the individual's circadian rhythms (schedules, sleep habits, physical activity, etc.)

Different chronotypes can be found depending on the person:

Depending on the bibliographic source, chronotypes are classified somewhat differently. The most direct and simple way to classify it would be:

Morning chronotype. People with a very high cognitive level in the morning that decreases throughout the day

Evening. Their cognitive functions are very high in the evening, so they tend to go to bed late and get up late.

Intermediate chronotype. There is no predilection for either the morning or the afternoon-evening.

As mentioned, it is a topic that is being studied frequently in recent years, especially in the influence on health with respect to weight variation. There are studies (5) that support an increase in weight and obesity with an inadequate breakfast, comparing it with lipid metabolization. Changes have also been observed in the metabolism of some macromolecules such as lipids. Plasma triglyceride concentrations are elevated during the night so that the postprandial response after an evening meal is increased with respect to a daytime intake. So it could be said that there are genes related to lipid metabolism and circadian rhythms. Studies such as that of Watanabe et al (6) showed that people who sleep little (less than 7 hours a day), increased the production of ghrelin (increased appetite) and suppressed leptin (hormone responsible for the regulation of appetite and thermogenesis), resulting in an increase in intake and thus an increase in the patient's BMI.

The timing, number of meals and intermittent fasting is a critical determinant of metabolic health. Improving patient education and raising awareness of the metabolic implications of the timing of meals should be part of the tools available to healthcare professionals in the fight against the current obesity epidemic. Obesity and weight gain are a global health concern right now on the planet. The prevalence of obesity is increasing dramatically and this public health problem needs to be addressed. The WHO (World Health Organization) has published some relevant and worrying statistical data. Since 1975, obesity has tripled, and in 2016 more than 1.9 billion adults were
overweight or obese (7), a figure that continues to rise today.

In Spain, 45.2% of children between 6 and 9 years of age are overweight or obese according to the ALADINO project (8).

Within the strategies for weight loss, some interventions have been seen that in principle would not require pharmacological treatment, which would be the control of dietary management and physical activity. In the purely food area, it is the individual’s job to take care of his or her diet, although the authorities in each country or region can help by means of labeling, advertising regulations and other options. If necessary, the help of a dietitian nutritionist can be very helpful in guiding the patient and providing nutritional education.

On the other hand, as regards physical exercise, we will be guided by the recommendations of the WHO (12), which has divided by age the estimated minimum time of physical activity necessary to obtain an adequate state of health. (These are general recommendations, for people with a normal level of health, without conditions or diseases)

Weight loss often does not come from an intentional way on the part of the person, but multiple factors may be involved, and in many occasions it does not occur intentionally.

However, the causes (10) can be quite diverse for weight loss to occur, such as:

- Tumors of the digestive system. The most common are those of the pancreas and liver, producing a lower food consumption and leading to weight loss.
- Lung cancer.
- Diabetes mellitus, especially of sudden onset, due to problems of insulin resistance and glycolytic (glucose-related) problems
- Hyperthyroidism.
- Depression and mental illness. There is usually a decrease in intake, and with it comes a decrease in intake.

Chrononutrition, the science that studies the effect of food on our circadian system, and weight loss, are two concepts that are being studied in depth in recent years, due to their possible importance in improving our state of health. The main objective of this literature review is to check whether factors such as meal timing, frequency, or fasting at certain times have an impact on weight loss.

Objectives.

**General Objective**
Gathering scientific evidence to see if circadian rhythms have an influence on weight loss

**Specific Objectives**
- Establish the relationship of meal timing and number of meals to weight loss
- Determine the effectiveness of correctly following circadian rhythms
- To see if different eating patterns (intermittent fasting, time-restricted eating), are effective in weight loss.

**Method**

In this literature review, a study on chrononutrition and weight loss is conducted. PubMed and Google Scholar were mainly used as databases.
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The search includes research studying both the relationship of circadian clocks and diet to beneficial and detrimental weight loss. We have tried to prioritize the search for clinical trials over other types of studies. However, meta-analyses, observational studies and others have also been used.

Specific inclusion and exclusion criteria were used: In terms of inclusion criteria:
- Articles from indexed journals, journals with an impact factor > 1.5 years maximum of research, articles mostly in English (75%) and the rest in Spanish (25%).

Regarding exclusion criteria:
- Titles that are not related to the subject to be studied, studies with insignificant or non-representative samples. On many occasions, the title may seem appropriate, but the content is not adequate and vice versa.

The search for items began in June 2023 and ended in August 2023. The databases used were:
- Pubmed. Keywords were used in the title and abstract. We used the Boolean operator "and. Together with Google Academic were the most used bases. Approximately 35 articles from this platform were used.
- ScienceDirect. Keywords were used in the title and abstract. The Boolean operator "and" was used. About 10 items used.
- Other sources:
  - Internet. Performed a search mainly for definitions to give figures and numbers. The introduction part is also where these pages have been used. About 7 articles (e.g. National Melatonin Institute, WHO, UN...)

Table 1. Methodology of the work. Own elaboration

<table>
<thead>
<tr>
<th>Part of the work</th>
<th>Search strategy</th>
<th>Number of items used</th>
<th>Number of items found</th>
<th>Databases and other sources used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>Weight loss</td>
<td>15</td>
<td>45</td>
<td>Google Scholar, Pubmed and internet sources</td>
</tr>
<tr>
<td>Meal frequency</td>
<td>Meal frequency and weight loss. The Boolean &quot;and&quot; Filter was used: Clinical trials mainly and 5 years old</td>
<td>4</td>
<td>140</td>
<td>Pubmed</td>
</tr>
<tr>
<td>Meal times</td>
<td>Weight loss and meal timing. The Boolean &quot;and&quot; was used. Filter: Clinical trials mainly and 5 years old</td>
<td>6</td>
<td>167</td>
<td>Pubmed</td>
</tr>
</tbody>
</table>
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Intermittent fasting

Weight loss and meal timing. The Boolean "and" was used. Filter: Clinical trials mainly and 5 years old

Results and Discussion

Frequency, schedule and intermittent fasting

Table 2. Table on meal timing and weight loss. Own elaboration

<table>
<thead>
<tr>
<th>Authors</th>
<th>Type of study</th>
<th>Weight loss efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruge T et al (13)</td>
<td>It is an observational study. A survey of eating habits of 1504 people over 18 years of age was used to explore the times and places where people ate.</td>
<td>According to the results of this study, people who ate meals later in the day had higher weight and BMI</td>
</tr>
<tr>
<td>Garaulet M et al (14)</td>
<td>Randomized clinical trial studying the effectiveness of weight loss in 420 individuals. 51% of the subjects ate early and 41% ate late. Intake, energy expenditure, appetite hormones, etc. were studied.</td>
<td>Late eaters lost less weight and showed a much slower rate of weight loss P(=0.002) (Short time constraint)</td>
</tr>
<tr>
<td>Purslow LR et al (15)</td>
<td>6764 men and women aged 40 to 75 years at baseline, daily food monitoring for 2 years, and objective weight and height measurements at baseline and at the end of the project</td>
<td>The lowest BMI was found in people who consumed more food at breakfast and gained much less weight than those who did not eat breakfast</td>
</tr>
<tr>
<td>Sievert K et al (16)</td>
<td>Review and meta-analysis of randomized clinical trials published between 1990 and January 2018. Of the 13 trials examined, 7 examined the effect of eating breakfast on weight change</td>
<td>Small difference in weight favored patients who skipped breakfast and ate at later hours. (95% Confidence Interval 0.007 to 0.82)</td>
</tr>
<tr>
<td>McCrory MA et al (17)</td>
<td>Review of 3 scientific literature studies</td>
<td>They see no clear effect on weight loss based on meal timing</td>
</tr>
</tbody>
</table>

6 210 Pubmed
Most of the studies show satisfactory results when meals are taken mostly in the early hours of the day (until approximately 3:00 p.m.) (13-15). However, not all studies were like this, they did not see significant differences in weight difference depending on the time of intake (16,17).

There is no certainty as to why it is better to eat earlier in the day. There are hypotheses of a possible slowing of metabolism when eating late in the day. Based on the relationship between circadian rhythms and weight loss, it seems that it may be due to the production of ghrelin (orexigenic hormone) according to research (13,15,17).

The regulation of food intake and energy balance is a complex process and is made possible by many endocrine signals, whereby the variables to be taken into account are very diverse.

The vast majority of the studies mentioned are trials, as they are the best way to test scientific theories, the empirical test. Meta-analyses are mentioned for their scientific quality in journals, although they have severe limitations. The number of studies analyzed are somewhat scarce, so that authors complain about the lack of clinical trials to demonstrate or clarify their effect (16,17,) in addition to the fact that the studies mentioned in this research are observational and therefore do not have the same certainty as randomized clinical trials.

The positive aspect of meta-analyses is the variety of conclusions and results of all the projects studied in order to be able to draw conclusions based on what has been studied (15). Garaulet M et al et al (14), in their clinical trials the follow-up and study time is relatively short. The time period of the investigations should be increased in order to obtain more accurate and objective results.

Table 3. Table on number of meals and weight loss. Own elaboration

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Weight loss efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paoli A et al (19)</td>
<td>Meta-analysis</td>
<td>To obtain a complete picture of the physiological and health effects of meal timing and frequency, multiple lines of research must be integrated, and an exploratory review seems, in our opinion, to be the appropriate approach to understand, at a glance, the influence of fasting, meal frequency and timing on cardiovascular disease</td>
</tr>
</tbody>
</table>
There is much disparity in the frequency of meals and weight loss, when it comes to reaching conclusions. Studies (19,20,23) support that a greater number of meals is involved in increased weight loss. On the other hand, Khaelova M et al (21) through their cohort study, affirm that it is better to have around 1 or 2 meals per day, as well as Maukonen and Grangeiro ED et al (20,23) bet on more meals per day due to other variables different from body weight.

what mechanisms promote weight loss depending on the number of meals you eat?

Meal timing and frequency are usually accompanied, so finding articles that mention this individually is difficult and as some studies mention (22), they would have to be compared with papers and research dealing with intermittent fasting and meal timing.

As a result, finding clinical trials proved difficult.

Nutritionists do not emphasize in consultation the number of meals to be taken per day, perhaps due to the complications that the subjects may have to take meals because of their work or their different chores.

In addition to weight (22), a greater number of meals distributed throughout the day improves other cardiovascular and metabolic parameters. More research is needed on this as they are secondary results, so there may have been flaws in the research. In contradiction, they verify a better lipid profile with a lower meal frequency, contrary to the studies of Paoli A and Ha Kyungho Ha et al (19,22). There are people who for different reasons cannot eat all their meals during the day, either because of their work, ethical, moral or other issues. A very important limitation is the pathophysiological status of the individuals. Khaelova M et al (21), in their research included obese people, smokers, with normal weight, so the result may be biased. Or other studies in which only women are included (19), so that the results of the study can sometimes not be comparable, due to the physiological and anatomical differences of the individuals. As
previously commented Paoli A et al (19), in their conclusions, claim that to see if there is a weight loss due to meal frequency would require future lines of research and to search for more current articles.

Other limitations would be the time of the studies. Those mentioned in the table above are not very recent (19,22), so recent articles of good quality would be desirable.

As before, the certainty in some studies is somewhat lower (23), due to the way the study methodology is carried out, which in the case of the Finnish comparative study, uses a 48h reminder to record dietary habits.

### Table 4. Intermittent fasting and weight loss

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Weight loss efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schubel R et al (29)</td>
<td>12-week randomized controlled trial, 3 groups (Group 1 deficit 75%, Group 2 deficit 20% and Group 3 no intervention)</td>
<td>Some weight loss in the fasting group, but it was not significant. In glucose levels, there was a difference in the non-fasting group.</td>
</tr>
<tr>
<td>Catenacci VA et al (25)</td>
<td>Randomized pilot study in 8 weeks of supervision. 2 groups. (Group 1 with no intake restriction and group 2 with a caloric restriction of 400 kcal per day)</td>
<td>Somewhat greater weight loss in people who were fasting.</td>
</tr>
<tr>
<td>Headland ML et al (30)</td>
<td>1-year randomized parallel trial. 3 groups (2 groups with continuous restriction and 1 group with intermittent fasting)</td>
<td>The weight loss results were: - 6.6 kg for the continuous restriction group, 5.1 kg for the group combining intermittent fasting and fasting and 5 kg for the normal group.</td>
</tr>
<tr>
<td>Lowe DA et al (28)</td>
<td>Randomized clinical trial of 116 overweight adults divided into 2 groups (Group 1 had only 3 meals and Group 2 had intermittent fasting)</td>
<td>The primary outcome sought was weight loss. The results do not show effective results in intermittent fasting.</td>
</tr>
<tr>
<td>Mandal et al (31)</td>
<td>Randomized controlled trial conducted in 101 obese and overweight adults with prediabetes</td>
<td>Intermittent fasting on alternate days was shown to have greater weight loss benefit than intermittent fasting.</td>
</tr>
<tr>
<td>Fiastuti Witjaksono et al (32)</td>
<td>Randomized clinical trial conducted in Jakarta, Indonesia. He was divided into a group that fasted twice a week and another group that did not fast.</td>
<td>Improvements in weight loss in the alternating fasting group.</td>
</tr>
</tbody>
</table>

Since intermittent fasting has been studied so recently, the number of 5-year studies is notorious, especially clinical trials, which are the most valuable in the field of medical sciences.
Studies (24,27,28) support the use of intermittent fasting for weight loss, but some, such as Jashmed H et al (26), do not mention weight loss in numerical terms, as does Headland ML et al (30), mentioning a somewhat greater difference, although not significant enough to affirm categorically the greater benefit of intermittent fasting with respect to normal caloric restriction.

Even so, intermittent fasting seems to have better results than a normal diet in terms of weight loss, in most cases, since lipid aspects and with glucose levels and so on, it would have to be studied more closely, and therefore this dietary tool is not recommended for some people.

In addition to weight loss, parameters such as glucose appear to undergo changes with intermittent fasting. Fasting glucose is lower during fasting; logically, as our glycogen reserves are used up, it can be recommended for diabetics, although more research is needed (29).

Another issue is whether alternate fasting or continuous fasting is better. Clinical trials (31,33) advocate alternate day fasting while (25) advocate intermittent fasting, in which fasting can sometimes be skipped. Although preached with weight loss, clinical trials such as the one of Lowe D.A. et al (28), mentions weight loss, but there is no decrease in BMI or lipid parameters so it may not be such a beneficial result because when weight is lost and it is not fat, it is usually water and body compounds. Other studies such as that of Headland ML et al (30) also show weight loss, but there is no significant difference with respect to the other groups in the study, whose weight loss is greater than in the case of fasting.

One of the most important limitations, as described for the other studies, is the pathophysiological situation of the subject. Many of the trials used are performed on obese patients, so comparing them to overweight or normal weight individuals is quite difficult, as the manner of weight loss with such heavy subjects is somewhat irregular and personal.

Another limitation with intermittent fasting is the fasting schedule. That is, if it is a 16 : 8, 8:16 etc., (16 hours of fasting, 8 hours of intake and 8 hours of fasting and 16 hours of intake, respectively). Most studies (25,27,29,30) do not mention the hours, as it also happens with alternate fasting, except for one research, which specifies the alternate fasting of 5:2 (29).

It is very difficult to find research that compares alternate and intermittent fasting in a single study to see which may be more suitable. Most of them were compared with a calorie-restricted diet (25,30,32). Alternate fasting is a type of fasting, which is performed sporadically or, rather, usually several days of fasting and then stop fasting for a few days.

Conclusions

This literature review analyzes the role of chrononutrition in weight loss structured in different blocks: frequency, schedule and fasting, through a literature review of about 50 studies, both national and international.

Emphasizing the studies analyzed, several conclusions can be drawn regarding meal frequency, meal timing and intermittent fasting. Regarding meal timing and weight loss, a large number of studies conclude that a higher intake earlier in the day is related to greater weight loss, although there are studies that do not support this hypothesis.

Continuing with the frequency of meals and weight loss, it is worth mentioning
that this is a more controversial topic than the previous one. Many studies look at meal frequency in conjunction with meal timing. There is more diversity of conclusions when studying meal frequency, one of the most frequent being that differences in parameters such as glucose, cholesterol or triglycerides can be seen when larger meals are consumed per day rather than weight loss benefits.

Finally, intermittent fasting, which is a way of eating that has become well-known in recent years. For a nutritionist, it should not be the first option to give because of its possible difficulty of adaptation for the individual. Most of the research found differences with respect to a normal diet with the same calories, especially in people who are overweight or obese. Even so, it is a diet for a specific population group that can cope well with fasting. In addition, it would be necessary to study how effective alternate or intermittent fasting is compared to continuous fasting.

Some of the aspects to be improved would be: to develop clinical trials with a large sample size. Studies should be conducted with a similar methodology to be as objective as possible. Nutritional education to the general population. Incentivize governments and public entities to invest in research and achieve greater studies over time.

As a final conclusion, the frequency, timing and number of meals are involved in weight loss on numerous occasions, without knowing the specific mechanism.

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