designs for health® Australia

Mastering Female Metabolic Health

Presenter: Kira Sutherland, Naturopathic Sports Nutritionist

Host: Tulsi Ryan, Nutritionist & Hebalist

Presenter | Kira Sutherland

überhealth

BHSc, Grad Dip Sports Nut, Adv Dip Nat, Adv Dip Nut, Adv Dip Herbal Med

Kira Sutherland is a Naturopath, Nutritionist, and Sports Nutritionist with more than 25 years of clinical practice. Her focus on performance nutrition led her to be the first Naturopath in Australia to undertake the International Olympic Committee's diploma in sports nutrition.

She was the 2019 winner of the BioCeuticals Integrative Medicine Award for Excellence in practice (Nutrition/Dietetics).

Kira divides her time between clinical practice, lecturing at the undergraduate level, and mentoring complementary medicine practitioners in applying holistic sports nutrition. In her free time, she competes in endurance sports and skis with her family as much as possible.

www.kirasuththerland.com.au @Uberhealth

Our Host | Tulsi Ryan

BHSc, DFH Health Educator

Tulsi Ryan is a Qualified Nutritionist and Herbal Medicine practitioner who provides health education services for Designs for Health practitioners. She also maintains her own natural health practice.

Tulsi has a special interest in:

- Practitioner education – making complex concepts easy to digest and apply in clinical practice.
- Gut health, mood and the gut-brain connection.
- Sports nutrition and body composition.

Tulsi will moderate the Q&A discussion for this webinar and engage our live Designs for Health Practitioner community to bring insights and practical clinical pearls for all.

Agenda

1. Insulin resistance and its drivers
2. Managing insulin resistance in female clients
3. Mitochondrial health, muscles and protein
4. Circadian rhythms and sleep hygiene influence metabolic health
5. Body types and seeing the whole picture
6. Action plan and questions

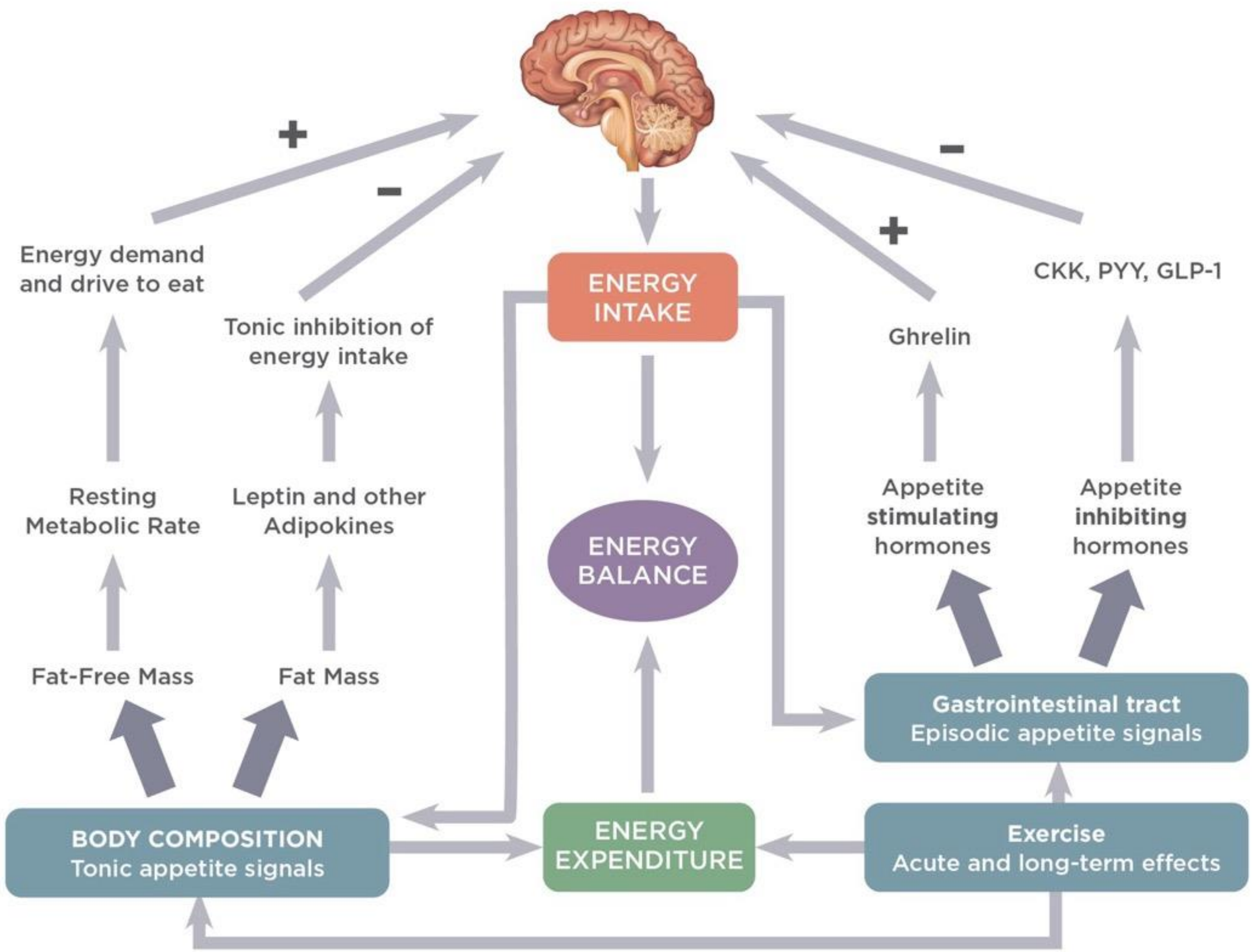
Insulin Resistance

A hormonal condition characterised by reduced sensitivity to insulin and chronically elevated levels of insulin. Also known as hyperinsulinemia and metabolic syndrome.

- Signs and symptoms
- Constant hunger
- Reactive hypoglycaemia
- Reduced ability to access fat stores for energy
- Higher blood pressure
- Increased risk of heart disease and dementia
- Higher triglycerides and lower HDL
- Higher CRP
- Fatty liver issues/disease
- Hypertrophied visceral fat/abdominal weight gain
- PCOS

How does insulin resistance cause higher hunger?

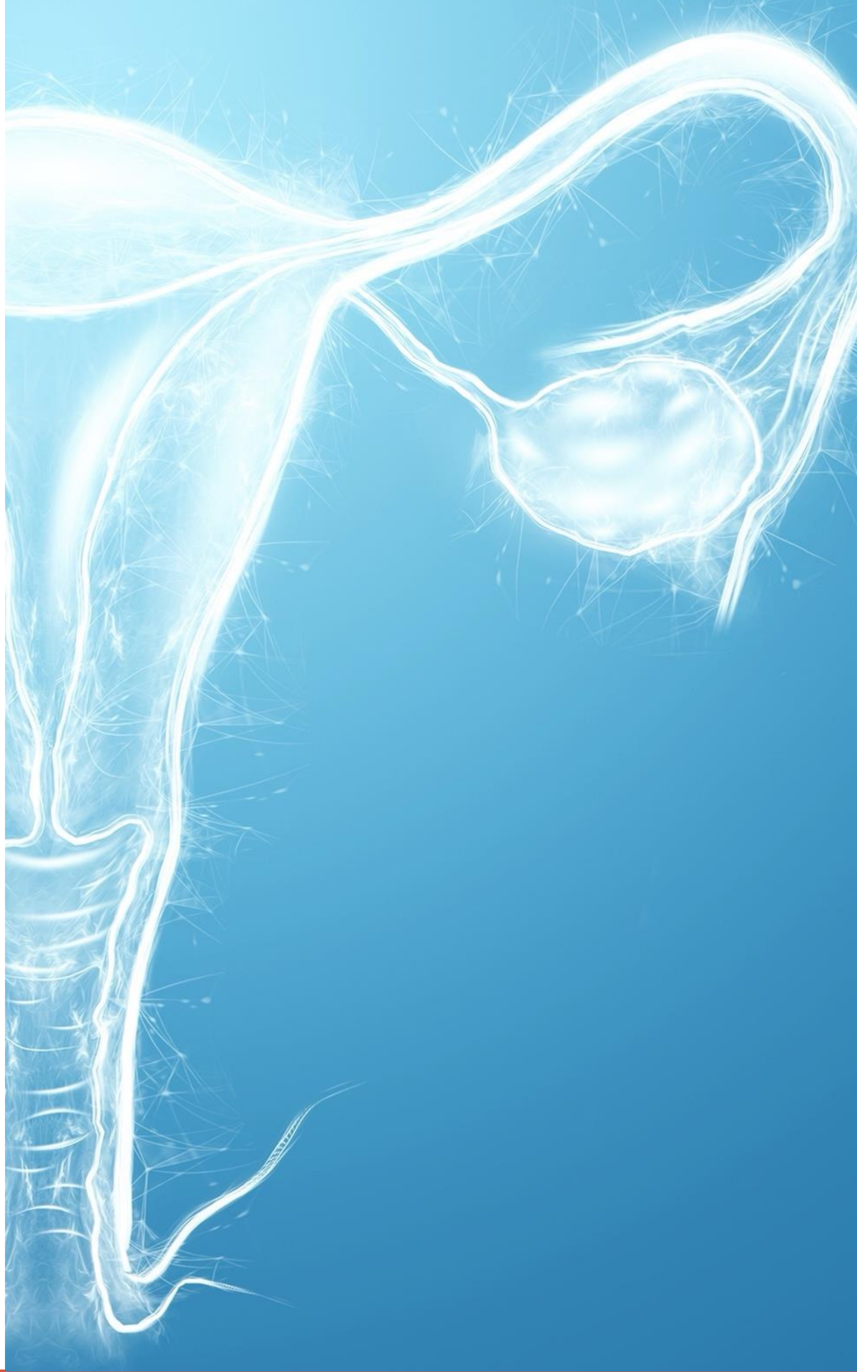
- Shifted fuel partitioning
- Disrupted satiety signalling via the hypothalamus
- Leptin resistance
- Reduced GLP-1 signalling
- Tendency to reactive hypoglycaemia
- Altered dopamine signalling, especially with ADHD



New formulation appetite. Formulation to show the separate effects of FFM and FM on the tonic drive to eat. Through a major influence on RMR, FFM reflects energy requirements of the body and is a driver of eating. FM reflecting the store of energy can modulate this drive but this is weakened as FM increases. Episodic influences on food intake arise, in part, from the action of food in the stomach and the periodic release of peptides from the gut after eating.

Female (AFAB) physiology

- Defends more strongly against subcutaneous fat loss.
- More likely to experience hypoglycaemia than males/AMAB.
- More vulnerable to hypothyroidism and autoimmune disease.
- Experience a monthly cycle with higher hunger and mild insulin resistance during the second half of the luteal phase.
- More prone to insulin resistance during perimenopause and beyond due to a lower hormone profile.



Recent research

- Hydrogen sulphide from gut dysbiosis damages the mitochondria of GLP-1 production cells. This can result in GLP-1 deficiency and can drive insulin resistance. (PMID 39030389)
- Androgen excess in females can promote insulin resistance and visceral fat gain. This is important for those with PCOS, peri-menopause and those taking androgenic progestins.
- Autoimmune thyroid disease increases the risk of hypertrophied visceral fat, fatty liver issues and insulin resistance. (PMID 35395842)

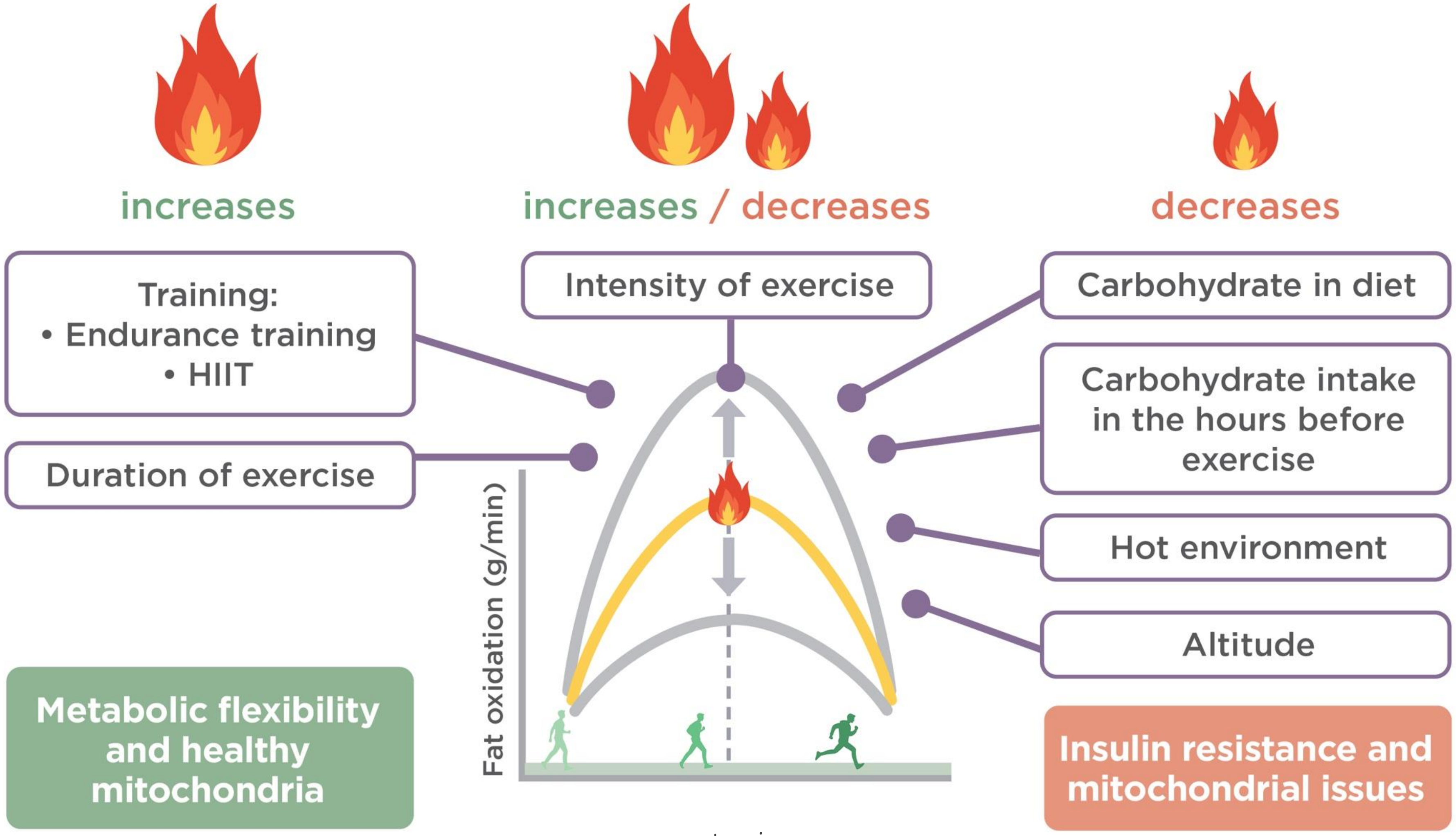
Visceral fat and fatty liver promote insulin resistance

- the hormone resistin
- accumulation of toxic lipid intermediates like ceramides
- impaired mitochondria
- ↑ gluconeogenesis
- ↓ glycogen storage

Insulin resistance promotes visceral fat and fatty liver

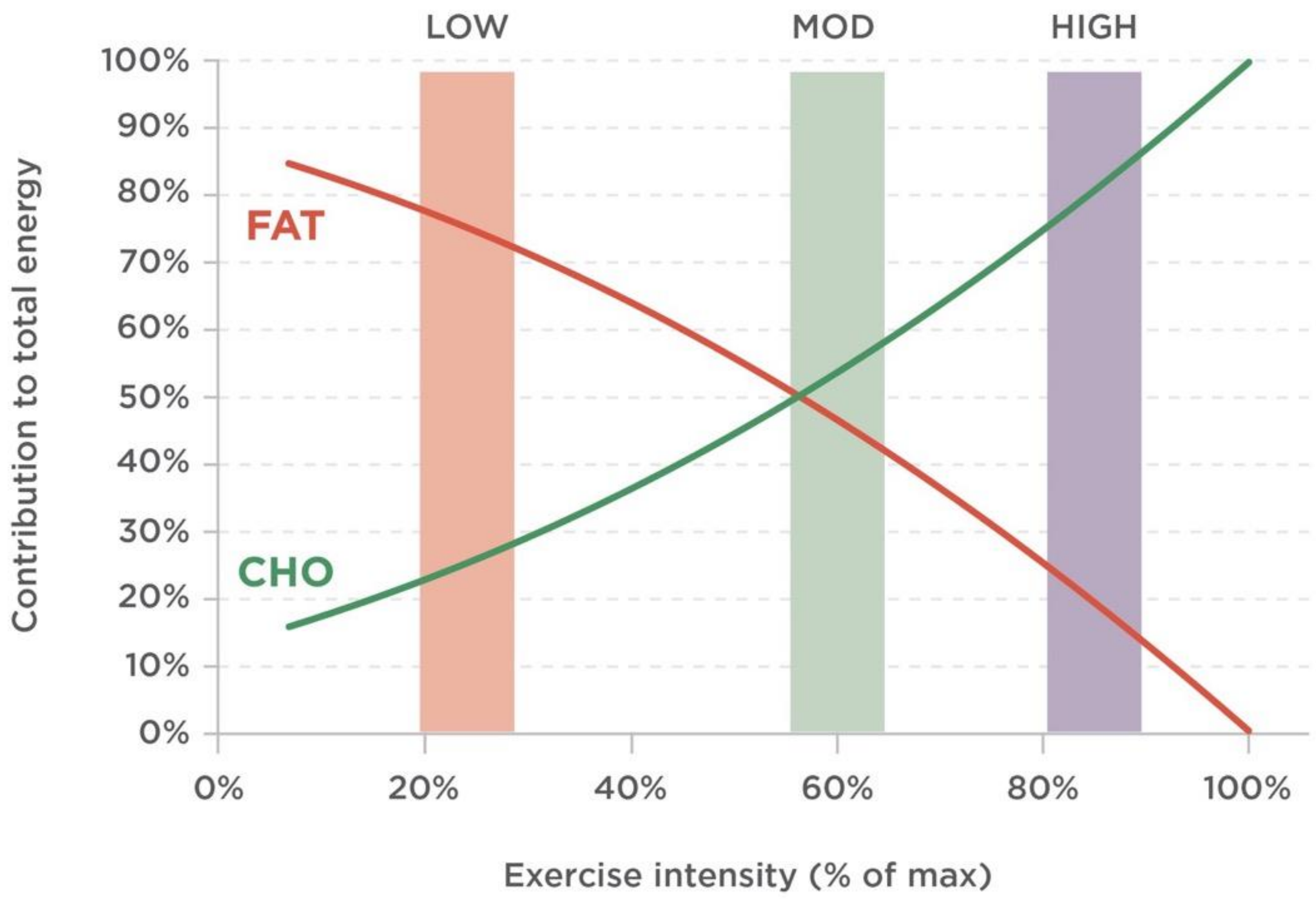
- ↑ fat storage
- ↑ de novo lipogenesis
- ↓ fat-burning
- ↑ inflammation
- ↓ adiponectin

Factors affecting fat oxidation during exercise



www.mysportsscience.com

Usage of carbohydrates and fat during exercise



(www.sportsscientists.com)

The contribution of CHO or lipids is influenced by:

- Exercise intensity/duration
- Diet prior to exercise
- High fat or high carb diet
- Substrate availability/ glycogen stores
- Training status
- Environmental factors
- Stress/cortisol
- Circadian alignment
- Genetics
- Sex
- Metabolic dysfunction and mitochondria

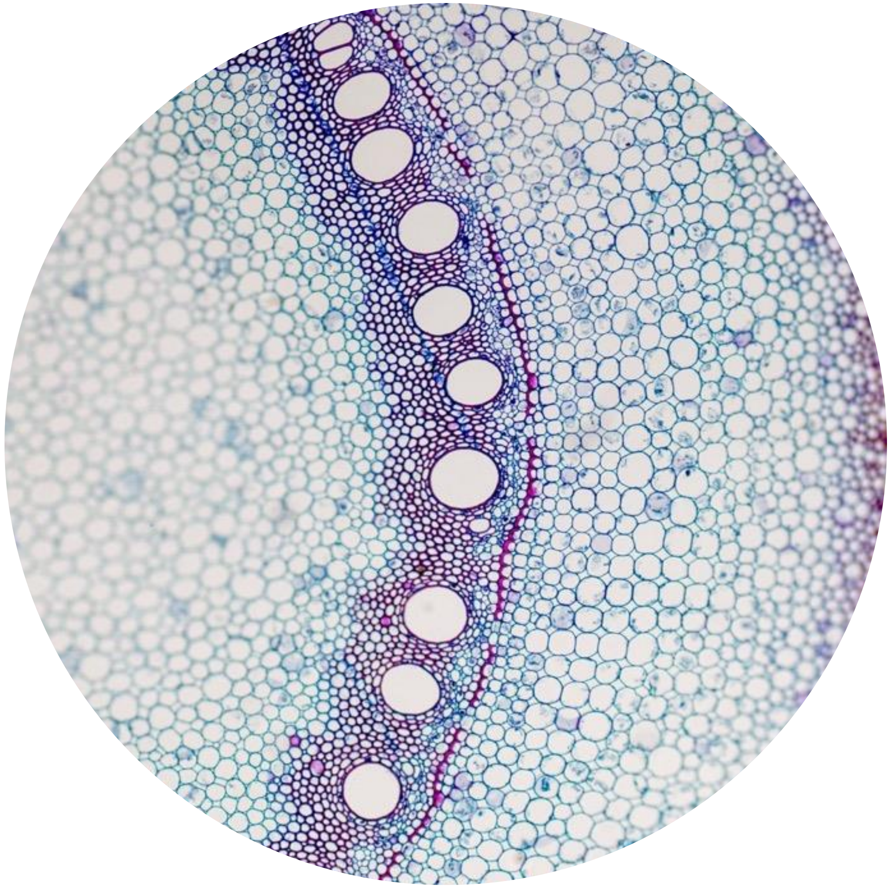
Mitochondria

- The largest number are within our muscles, liver, brain and heart.
- They produce approximately 90% of cellular energy.
- Dysfunction of mitochondria creates a reduction in energy production (ATP) and a reduced efficiency of the electron transport system.

(Nicholson, 2014) (Du, 2016)

Mitochondrial functions

- The only place we burn fat as a fuel for ATP.
- Also burns carbohydrates and protein.
- Amino acid metabolism and homeostasis.
- Apoptosis and autophagy regulation.
- Calcium homeostasis and membrane potential.
- Immune system function.
- Iron metabolism and heme synthesis.
- Regulator of neurotransmitter signaling.
- Steroid synthesis.
- Thermogenesis.



Issues of energy production

- Dysfunction in the mitochondria creates issues with aerobic respiration and a move to anaerobic pathways.
- Increased fatigue and less fat being burned as fuel.

(Delacruz, Mitochondrion. 2018;41:37-44.)

ORIGINAL PAPER

WILEY Aging Cell

Metformin inhibits mitochondrial adaptations to aerobic exercise training in older adults

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Abstract

Metformin and exercise independently improve insulin sensitivity and decrease the risk of diabetes. Metformin was also recently proposed as a potential therapy to slow aging. However, recent evidence indicates that adding metformin to exercise antagonizes the exercise-induced improvement in insulin sensitivity and cardiorespiratory fitness. The purpose of this study was to test the hypothesis that metformin diminishes the improvement in insulin sensitivity and cardiorespiratory fitness after aerobic exercise training (AET) by inhibiting skeletal muscle mitochondrial respiration and protein synthesis in older adults (62 ± 1 years). In a double-blinded fashion, participants were randomized to placebo (*n* = 26) or metformin (*n* = 27) treatment during 12 weeks of AET. Independent of treatment, AET decreased fat mass, HbA1c, fasting plasma insulin, 24-hr ambulant mean glucose, and glycemic variability. However, metformin attenuated the increase in whole-body insulin sensitivity and VO_2max after AET. In the metformin group, there was no overall change in whole-body insulin sensitivity after AET due to positive and negative responders. Metformin also abrogated the exercise-mediated increase in skeletal muscle mitochondrial respiration. The change in whole-body insulin sensitivity was correlated to the change in mitochondrial respiration. Mitochondrial protein synthesis rates assessed during AET were not different between treatments. The influence of metformin on AET-induced improvements in physiological function was highly variable and associated with the effect of metformin on the mitochondria. These data suggest that prior to prescribing metformin to slow aging, additional studies are needed to understand the mechanisms that elicit positive and negative responses to metformin with and without exercise.

KEYWORDS
aging, healthspan, protein synthesis, proteostasis, telomere

Insulin Resistance and the Mitochondrial

- Stress and sleep deprivation cause oxidative damage to mitochondria.
- High blood glucose increases production of ROS.
- Increased ROS inhibits insulin signalling pathways and interferes with the oxidation of Acetyl CoA.
- Increasing lipid and free fatty acid deposition in insulin-target tissues.
- Contributing to metabolic dysfunction, obesity, type 2 diabetes and potentially PCOS.

(Doi:10.1016/bs.pmbts.2016.12.012)

Damage to the mitochondria

- Alcohol, smoking.
- Pesticides, antibiotics.
- Statins, paracetamol.
- Lack of movement, loss of muscle.
- Vegetable oils (Omega 6).
- Overeating, high fructose corn syrup.
- Certain food choices.
- Circadian misalignment.

Modern dietary issues

- Lower protein intake.
- Lower fibre intake.
- Missing/lowered micronutrient status.
- Additives and emulsifiers.
- High fructose intake.
- Higher omega-6 intake.
- Hyper processed foods.
- Hyper palatable foods (sweet and salt).

Poor mitochondrial function is linked to:

- Aging
- Alzheimer’s and Parkinson's disease
- Atherosclerosis, Cardiovascular disease
- Chronic fatigue, exhaustion
- **Insulin resistance, metabolic issues, and obesity**
- Kidney damage
- Depression and some psychiatric disorders
- Diabetes
- **Fatty liver disease, NAFLD**
- Fibromyalgia
- Neurodegenerative disorders

Mitochondria Support

1. Healthy insulin levels
2. Oestrogen and progesterone
3. Adequate melatonin production
4. Healthy thyroid function
5. Exercise and movement
6. Build and maintain muscle mass
7. Intermittent fasting, ketogenic diet
8. Energy restriction,
   fat adaptation exercise and diet
9. Circadian rhythm alignment
10. Adequate sleep/rest
11. Stress management
12. Mitochondrial nutrients

Du J, et al, 2016) (Di Lorenzo, 2020; Garrido-Maraver, 2014) (doi: 10.1080/10408398.2013.876960)

Body types, circadian rhythms and metabolic health

Body types and metabolic health

- You cannot assess insulin resistance via body size.
- Genetics play a key role in body shape, size and circadian rhythm.
- Different body types require different metabolic strategies, food and exercise programs.

Blood results that suggest insulin resistance:

- triglycerides > 1.7 mmol/L (150 mg/dL)
- urate > 0.33 mmol/L
- C-RP > 1 mg/L
- ALT > 19 IU/L
- serum ferritin > 200 ng/mL

Insulin readings that indicate insulin resistance

- fasting insulin > 8 mIU/L or 55 pmol/L
- 1 or 2-hour insulin > 60 mIU/L or 410 pmol/L
- HOMA-IR index > 1.0
- *If insulin is high, it's insulin resistance. If it's low, you just don't know.*

Exercise and Movement

The effect of exercise on glucose responses lasts many days:

- Glucose response to a meal the days after exercise
- This makes interpretation of CGM data more challenging

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Sarcopenia & mitochondria

- Sarcopenia = loss of mitochondrial numbers.
- Maintain muscle mass = maintain mitochondrial numbers and function, slows aging.
- Periodized aerobic training in a low-carb state (1-2 times per week) can activate mitochondrial biogenesis pathways. (Bartlett et al., 2015)
- Resistance/strength training 2-3 times a week to maintain muscle.
- Adequate protein intake to maintain muscle mass.

Exercise benefits glucose and lipid metabolism, skeletal muscle function and growth, maintains bone density and assists insulin sensitivity in adipose tissue.

Exercise and mood improvement

- Exercise has been shown to be just as potent as that of serotonergic medications. *(Babyak, 2000)*
- Causes acute increases in levels of endorphins and BDNF.
- Decreases resting levels of cortisol and alters brain levels of neurotransmitters, including serotonin, dopamine and adrenaline.
- Many sports are also social in nature, thus increasing serotonin, dopamine, and oxytocin.
- Structural brain changes in areas such as the hippocampus, anterior cingulate cortex, prefrontal cortex, striatum, and amygdala may also mediate the benefits of exercise on mood and depression.

(examine.com/2023)

To counteract sarcopenia

Resistance training is the most potent and cost-effective treatment to prevent sarcopenia

Leucine at >4.5gm per day in conjunction with strength training

Protein intake 1.6-2.0gm/kg/day or higher to maximally stimulate MPS

Creatine, adequate vitamin D and Omega 3's

(Thomas, Erdman, Bure, 2016) (Phillips, 2012) (Mettler, Mitchell, Tipton, 2010)(Phillips, Van Loon, 2011)

Optimal daily protein intake for adults in grams per kilogram of body weight (g/kg)

	Maintenance	Muscle gain	Fat loss			
Sedentary	≥1.2*			1.2–1.5	1.66–1.77	>1.5
Active	1.4–1.6**	1.4–2.4***	1.8–2.7***		unknown	unknown

* Keep in mind that you'll get better body composition results by adding consistent activity than merely by hitting a protein target.
** People who are trying to keep the same weight but improve their body composition (more muscle, less fat) may benefit from the higher end of the range.
*** For experienced lifters, intakes up to 3.3 g/kg may help minimize fat gain while bulking.

Examine.com

Modern dietary issues

- Lower protein intake
- Lower fibre intake
- Missing/lowered micronutrient status
- Additives and emulsifiers
- High fructose intake
- Higher omega-6 intake
- Hyper processed foods
- Hyper palatable foods (sweet and salt)

Metabolic Nutrients

Magnesium

- Regulates mitochondrial membrane potential.
- Supports glucose transporter protein.
- Reduces inflammation and supports inositol and thiamine.
- Enhances insulin receptor function.
- Improves insulin sensitivity, stabilises blood sugar, and prevents reactive hypoglycaemia.

- Dosage: 300mg and up

Metabolic Nutrients

Inositol

- Breaks down fat.
- Prevents and treats fatty liver.
- Lowers androgens.
- Improves mitochondrial health and insulin sensitivity.
- Supports thyroid function.
- Boosts dopamine, acetylcholine, GABA and serotonin.

- Dosage: 2000-6000mg in split dosages

Myo-Inositol

- **Myo-inositol significantly improves insulin sensitivity in women with PCOS and metabolic syndrome:**
  Multiple clinical trials show that supplementation with myo-inositol (typically 2–4g/day) leads to improved HOMA-IR scores, reduced fasting insulin, and better glucose tolerance – particularly in women with polycystic ovary syndrome.
- **Myo-inositol supports hormonal balance and ovulation in PCOS:**
  Myo-inositol helps restore normal ovulatory function, reduce serum androgen levels, and improve menstrual regularity in women with PCOS, making it a valuable fertility support nutrient.
- **Reduces gestational diabetes risk and improves pregnancy outcomes:**
  In pregnant women at risk of gestational diabetes mellitus (GDM), myo-inositol supplementation reduced GDM incidence, improved insulin sensitivity, and lowered the need for insulin therapy, without adverse effects.

(DiNicolantonio et al,2022 & Unfer et al, 2017)

Berberine

- **Improved Glycaemic Control:** Berberine supplementation significantly reduced fasting blood glucose (FBG) and glycated haemoglobin (HbA1c) levels in women, particularly for women that are peri or post menopausal, with PCOS & metabolic syndrome.
- **Enhanced Insulin Sensitivity:** by decrease in the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) among female participants, suggesting improved insulin sensitivity.
- **Lipid Profile Benefits**: Women experienced reductions in total cholesterol and low-density lipoprotein (LDL) cholesterol levels, contributing to better cardiovascular health.
- **Safety Profile:** Berberine was generally well-tolerated among female participants, with no significant adverse effects reported.

Ye et al, 2021, Zhao et al, 2023

B Vitamins

- Deficiencies in vitamin B6 (pyridoxal 5′-phosphate) B12 and folate—and subsequent hyperhomocysteinemia—may contribute to the development of insulin resistance, endothelial dysfunction, and systemic inflammation, offering therapeutic potential through targeted nutritional interventions.
- Elevated homocysteine is a result of impaired one-carbon metabolism via methylation, which relies on adequate levels of folate B6 and vitamin B12 as essential cofactors.
- Disruption in this pathway can lead to **endothelial dysfunction, oxidative stress, and systemic inflammation**, all of which are implicated in the development of metabolic syndrome and insulin resistance.
- Elevated homocysteine levels are known to increase the generation of reactive oxygen species (ROS) and activate **NF-κB**, a key transcription factor in the inflammatory response.
- This contributes to **chronic low-grade inflammation** observed in metabolic syndrome, further exacerbating insulin resistance and cardiovascular risk.
- Optimal B vitamin status may offer **protective effects** against the development of insulin resistance, abdominal obesity, dyslipidemia, and hypertension.

(Ulloque-Badaracco et al, 2023 & Zhu et al, 2023)

Fibre

- Adequate dietary fibre is associated with improved insulin sensitivity and favourable changes in body composition and weight.
- Higher dietary fibre intake is associated with lower insulin resistance, as measured by the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).
- Improves glucose metabolism: Soluble fibre slows gastric emptying and carbohydrate absorption, leading to lower postprandial glucose spikes and improved insulin sensitivity.
- Modulates gut microbiota: Fermentable fibres enhance short-chain fatty acid (SCFA) production (especially butyrate), which has anti-inflammatory effects and improves insulin signalling.
- **Reduction in systemic inflammation:** Increased fibre intake is associated with lower inflammatory markers (e.g., CRP), which are known to impair insulin receptor function.
- **Improve satiety and body composition:** Fibre contributes to appetite regulation and reduced caloric intake, leading to weight loss—indirectly improving insulin sensitivity via decreased adiposity.
- Fibers such **as β-glucan, psyllium**, and **guar gum, inulin, acacia, apple pectin, beta glucan, psyllium husk , flaxseed** (which are viscous and fermentable) were shown to significantly lower fasting glucose and improve HOMA-IR scores.
- These fibres slow gastric emptying and form gels that reduce postprandial glucose excursions, thereby reducing insulin demand and improving sensitivity.

(Hall et al, 2024 & Xiang et al, 2025)

Collagen Peptides

- The collagen peptides have been shown to exert antioxidant effects and antiglycation activity, helping to neutralise reactive carbonyl species that drive advanced glycation end products (AGE’s) formation.
- This is relevant to improving **insulin sensitivity and metabolic resilience**, particularly in aging or metabolically challenged individuals.
- 13g / day has been shown to reduce levels of fasting glucose, triglyceride, and free fatty acids.
- Microbiome effect in beneficially altering firmicutes: Bacteroidetes ratio, which have an anti-obesogenic effect.

Other nutrients to consider

- Taurine
- Choline
- Glycine
- CoQ10
- Other mitochondrial supporting nutrients
- Liver and digestive herbs and nutrients

ARTICLE OPEN

Check for updates

Taurine reduces the risk for metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials

Chih-Chen Tzang[1], Liang-Yun Chi[1], Long-Huei Lin[2], Ting-Yu Lin[3], Ke-Vin Chang[4,5,6], Wei-Ting Wu[4,5] and Levent Özçakar[7]

BACKGROUND: Metabolic syndrome (MetS) is a cluster of interconnected risk factors that significantly increase the likelihood of cardiovascular disease and type 2 diabetes. Taurine has emerged as a potential therapeutic agent for MetS. This meta-analysis of randomized controlled trials (RCTs) aimed to evaluate the effects of taurine supplementation on MetS-related parameters.
METHODS: We conducted electronic searches through databases like Embase, PubMed, Web of Science, Cochrane CENTRAL, and ClinicalTrials.gov, encompassing publications up to December 1, 2023. Our analysis focused on established MetS diagnostic criteria, including systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C). Meta-regression explored potential dose-dependent relationships based on the total taurine dose administered during the treatment period. We also assessed secondary outcomes like body composition, lipid profile, and glycemic control.
RESULTS: Our analysis included 1024 participants from 25 RCTs. The daily dosage of taurine in the studies ranged from 0.5 g/day to 6 g/day, with follow-up periods varying between 5 and 365 days. Compared to control groups, taurine supplementation demonstrated statistically significant reductions in SBP (weighted mean difference [WMD] = −3.999 mmHg, 95% confidence interval [CI] = −7.293 to −0.706, $p = 0.017$), DBP (WMD = −1.509 mmHg, 95% CI = −2.479 to −0.539, $p = 0.002$), FBG (WMD: −5.882 mg/dL, 95% CI: −10.747 to −1.018, $p = 0.018$), TG (WM
HDL-C (WMD: 0.644 mg/dl, 95% CI: −0.244 to 1.532, $p = 0.155$
DBP (coefficient = −0.0108 mmHg per g, $p = 0.0297$) and FBG (coefficient = −0.0445 mg/dL per g, $p = 0.0273$). No significant

Tzang CC et al. Taurine reduces the risk for metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. Nutr Diabetes. 2024;14:29. PMID: 38755142

Reasons for weight gain

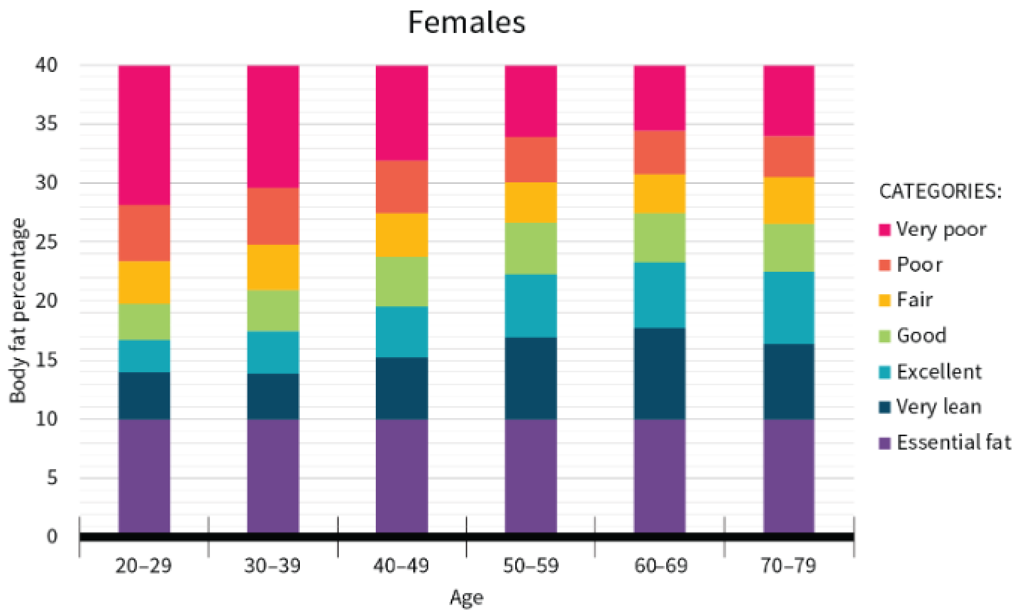
- Gut dysbiosis
- Chronic inflammation
- Thyroid and hormone issues
- **Insulin resistance, fatty liver**
- Medications (OCP, antidepressants etc.)
- Lack of exercise, sedentary lifestyle
- Mitochondrial issues
- **Adaptive thermogenesis**
- **Circadian dysregulation**
- **Genetic predisposition**
- Excess of calories eaten vs expenditure

Parameters to measure

Get a baseline of your measurements, just like we do with hormones:

- Weight (best in kilos)
- Body measurements (chest, waist, bum/hips)
- Lean body mass/muscle mass
- Body fat (19-32% considered healthy)
- DEXA, bioimpedance or bodpod
- Resting metabolic rate (RMR)
- Blood glucose levels (CBG Monitors)
- Food and training diaries
- **Learn your body type/somatotype**

Female body composition categories based on age and percentage of body fat.



Adapted from American College of Sports Medicine. Body Composition (chapter 5 in *ACSM's Health-Related Physical Fitness Assessment Manual, 4th ed.* Lippincott Williams & Wilkins. 2013. ISBN:978-1451115680)

Adaptive Thermogenesis (AT)

- The metabolic alteration to minimise the degree of energy deficit created by continual energy restriction (CER).

- One study found a decrease in total daily energy expenditure (TDEE) by 6-18% due to AT.
- Decrease thyroid hormones (T3 and T4).
- Change in appetite-regulating hormones (ghrelin/leptin).
- Potential increase in cortisol.
- Do not under fuel!

Cycles and rhythms

- Cyclical dieting.
- Brain chemistry/triggering famine hormones (AT).
- Circadian rhythms of mealtimes.
- Menstrual cycle alterations in fuel usage.
- Chronotype influence on digestion, stress, sleep and mealtimes.
- Eating pre and post exercise for optimal insulin response.

ized Controlled Trial > Int J Obes (Lond). 2018 Feb;42(2):129-138.
38/ijo.2017.206. Epub 2017 Aug 17.

mittent energy restriction improves weight loss ency in obese men: the MATADOR study

[1 2], A Sainsbury [3], N A King [2], A P Hills [1 2], R E Wood [1 2]

+ expand

25405 PMCID: PMC5803575 DOI: 10.1038/ijo.2017.206

article

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nd/objectives: The MATADOR (Minimising Adaptive Thermogenesis And Deactivating ebound) study examined whether intermittent energy restriction (ER) improved weight loss compared with continuous ER and, if so, whether intermittent ER attenuated compensatory associated with ER.

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

BRIEF REPORT

Differential effects of the circadian system and circadian misalignment on insulin sensitivity and insulin secretion in humans

Jingyi Qian PhD, Chiara Dalla Man PhD, Christopher J. Morris PhD, Claudio Cobelli PhD, Frank A. J. L. Scheer PhD

First published: 04 June 2018 | https://doi.org/10.1111/dom.13391 | Citations: 67

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Chiara Dalla Man and Christopher J. Morris contributed equally to the study.

Greater caloric intake at breakfast versus dinner promotes:

- Weight loss and insulin sensitivity.
- Improves fasting glucose levels.
- Better blood lipid profiles.
- Gastric emptying rates peak in the morning.
- Beta-cell function can be up to 15% higher in the morning.
- Greater glucose fluctuations after eating in the evening.

Published in final edited form as:
Int J Obes (Lond). 2019 August ; 43(8): 1644–1649. doi:10.1038/s41366-018-0208-9.

Ghrelin is Impacted by the Endogenous Circadian System and by Circadian Misalignment in Humans

Jingyi Qian[1], Christopher J Morris[1], Rosanna Caputo[1,2], Marta Garaulet[3], Frank AJL Scheer[1]

[1]Medical Chronobiology Program, Division of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women's Hospital, Boston, MA; Division of Sleep Medicine, Department of Medicine, Harvard Medical School, Boston, MA, USA. [2]Division of Neurophysiology, Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, Netherlands. [3]Chronobiology Laboratory, Department of Physiology, University of Murcia and Research Biomedical Institute of Murcia, Murcia, Spain.

Abstract

The human circadian system regulates hunger independently of behavioral factors, resulting in a trough in the biological morning and a peak in the biological evening. However, the role of the only known orexigenic hormone ghrelin in this circadian rhythm is unknown. Furthermore, although shift work is an obesity risk factor, the separate effects of the endogenous circadian system, the behavioral cycle, and circadian misalignment on ghrelin has not been systematically studied. Here we show—by using two 8-d laboratory protocols—that circulating active (acylated) ghrelin levels are significantly impacted by endogenous circadian phase in healthy adults. Active ghrelin levels were higher in the biological evening than the biological morning (fasting +15.1%, P=0.0001; postprandial +10.4%, P=0.0002), consistent with the circadian variation in hunger (P=0.028). Moreover, circadian misalignment itself (12-h behavioral cycle inversion) increased postprandial active ghrelin levels (+5.4%; P=0.04). While not significantly influencing hunger (P>0.08), circadian misalignment increased appetite for energy-dense foods (all P<0.05). Our results provide possible mechanisms for the endogenous circadian rhythm in hunger as well as for the increased risk of obesity among shift workers.

High Caloric Intake at Breakfast vs. Dinner Differentially Influences Weight Loss of Overweight and Obese Women

Daniela Jakubowicz,[1] Maayan Barnea,[2] Julio Wainstein,[1] Oren Froy[2]

Objective: Few studies examined the association between time-of-day of nutrient intake and the r
bolic syndrome. Our goal was to compare a weight loss diet with high caloric intake during breakfa
an isocaloric diet with high caloric intake at dinner.
Design and Methods: Overweight and obese women (BMI 32.4 ± 1.8 kg/m^2) with metabolic sync
were randomized into two isocaloric (~1400 kcal) weight loss groups, a breakfast (BF) (700 kcal b
fast, 500 kcal lunch, 200 kcal dinner) or a dinner (D) group (200 kcal breakfast, 500 kcal lunch, 700
dinner) for 12 weeks.
Results: The BF group showed greater weight loss and waist circumference reduction. Although fa
glucose, insulin, and ghrelin were reduced in both groups, fasting glucose, insulin, and HOM
decreased significantly to a greater extent in the BF group. Mean triglyceride levels decreased by 3
in the BF group, but increased by 14.6% in the D group. Oral glucose tolerance test led to a g
decrease of glucose and insulin in the BF group. In response to meal challenges, the overall daily
cose, insulin, ghrelin, and mean hunger scores were significantly lower, whereas mean satiety s
were significantly higher in the BF group.
Conclusions: High-calorie breakfast with reduced intake at dinner is beneficial and might be a u
alternative for the management of obesity and metabolic syndrome.

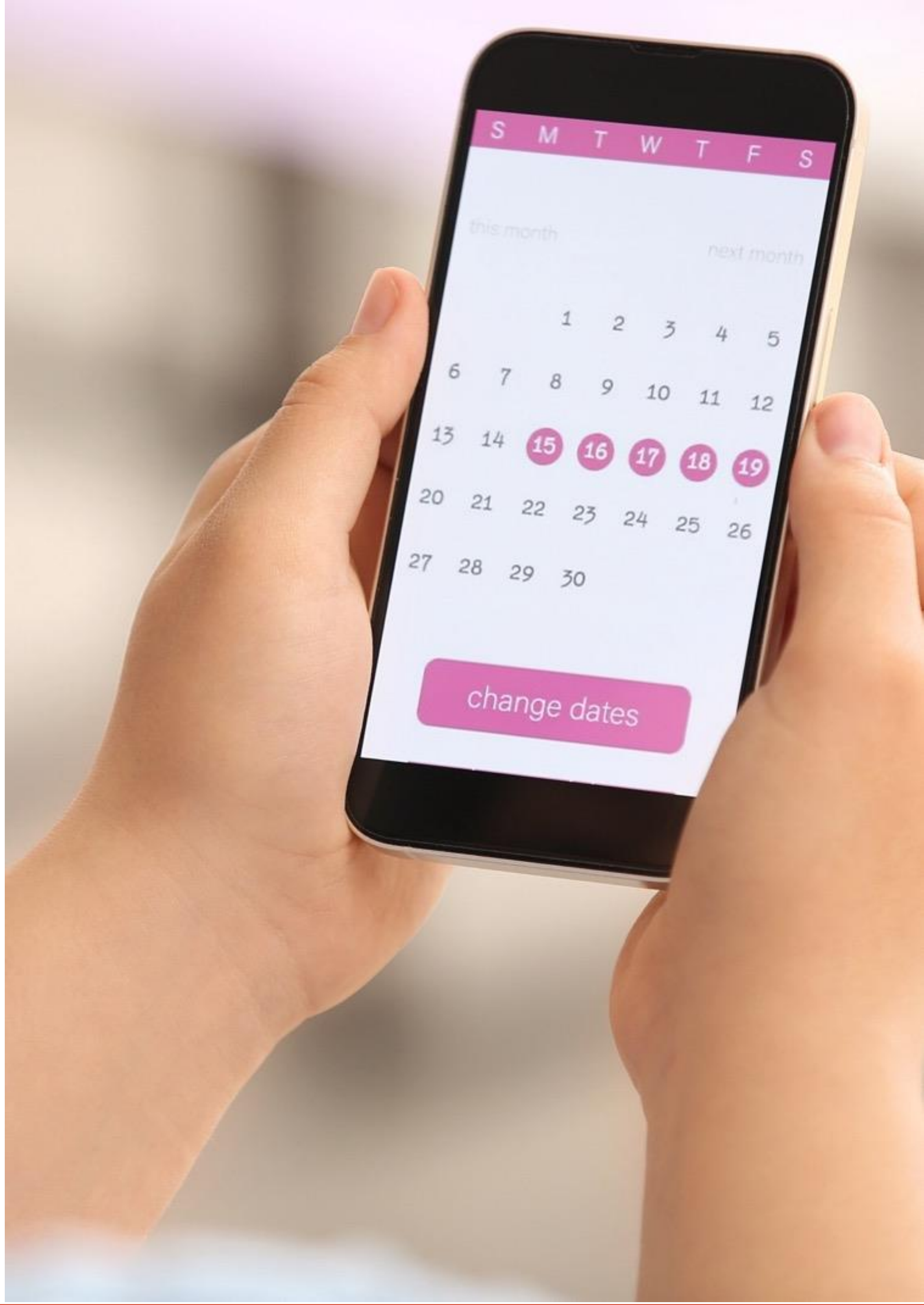
Obesity (2013) **00**, 000–000. doi:10.1002/oby.20460

doi.org/10.1016/0016-5085(87)90913-9, doi.org/10.1111/dom.13391, doi.org/10.1210/edrv.18.5.0317

Tailoring diet to the cycle

- Studies suggest that oestrogen has an inhibitory effect on energy intake, and progesterone can mitigate this.
- When progesterone is elevated in the LP it has been shown to promote fat storage, increase appetite and cravings.
- The premenstrual drop in oestrogen and dopamine can trigger binge eating, especially in those with ADHD or a tendency to lower dopamine levels.

- It is proposed that insulin sensitivity is lower in the luteal phase. *(Davidson et al, 2007)*
- Commencing diets in the follicular phase to avoid the LP cravings.
- Idea of cyclical dieting (2 weeks on, 2 weeks off).

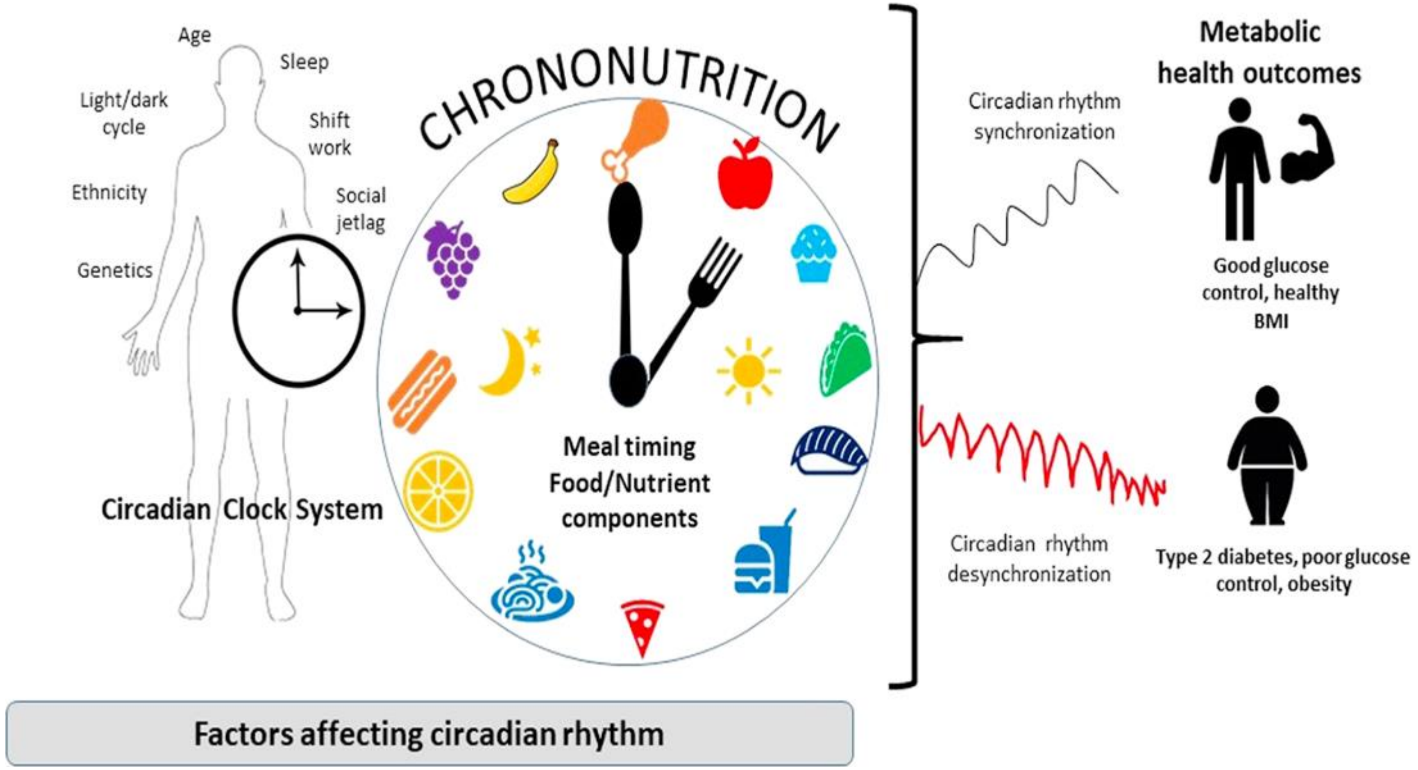


Why is Chronobiology Important

To understand WHEN our body should rest or be exposed to stress/exercise etc.

It influences:

- Energy/fatigue levels
- Digestive function/symptoms
- Hormonal balance
- Stress levels
- Body composition
- Mental health & immunity
- Development of chronic disease



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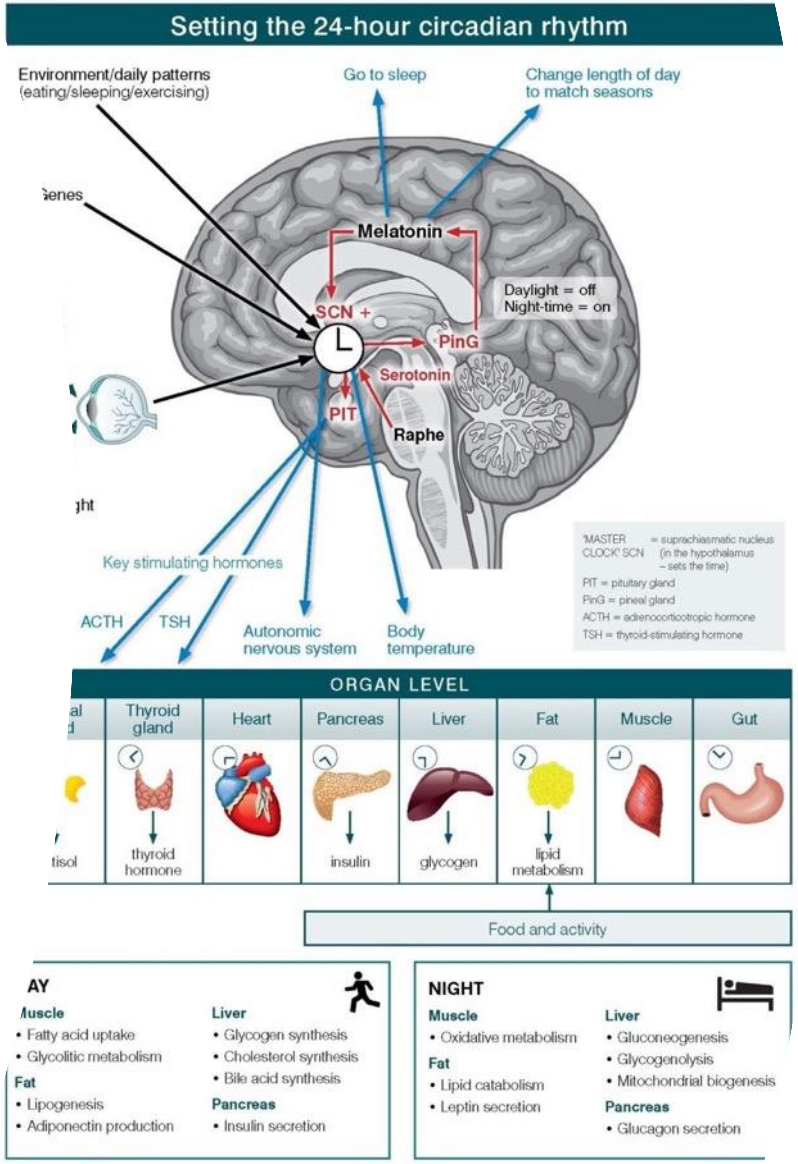
Altered Eating and Sleeping Patterns

- Circadian misalignment.
- Decreases leptin and increases ghrelin levels.
- Increases glucose and insulin level.
- Disrupts the cortisol rhythm.
- Affecting endocrine and adipose tissue metabolism.
- Decreases fat oxidation and increases carb dependence.
- Inhibit muscle gains from exercise.
- Increases inflammation and blood pressure.

- Decreases heart rate variability (HRV), which shows the interplay between the sympathetic and parasympathetic nervous system.



(bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-11-79)

Circadian Rhythm & Metabolic Health

- Circadian-rhythm disruption is a risk factor for metabolic health.
- In a 6-week intervention, women restricted to an average of **5.6 hours of sleep per night** exhibited a **significant reduction in whole-body insulin sensitivity**, measured via frequently sampled intravenous glucose tolerance tests (FSIGTs).
- Sleep restriction may impair insulin signalling via increased sympathetic activity, elevated evening cortisol, systemic inflammation, and disruption of **circadian gene expression (e.g., CLOCK, BMAL1, PER, CRY),** which are integral to metabolic regulation.
- The increase in insulin resistance occurred **independently of weight gain**, suggesting that sleep loss exerts **direct physiological effects** on glucose metabolism through neuroendocrine and circadian pathways.
- The decline in insulin sensitivity was **more pronounced in postmenopausal participants**, implicating estrogen deficiency and age-related metabolic shifts as potential amplifiers of sleep-related insulin dysregulation.

(Schrader etal, 2015 & Zuraikat et al, 2023)

We Have Differences in Our Optimal Stress

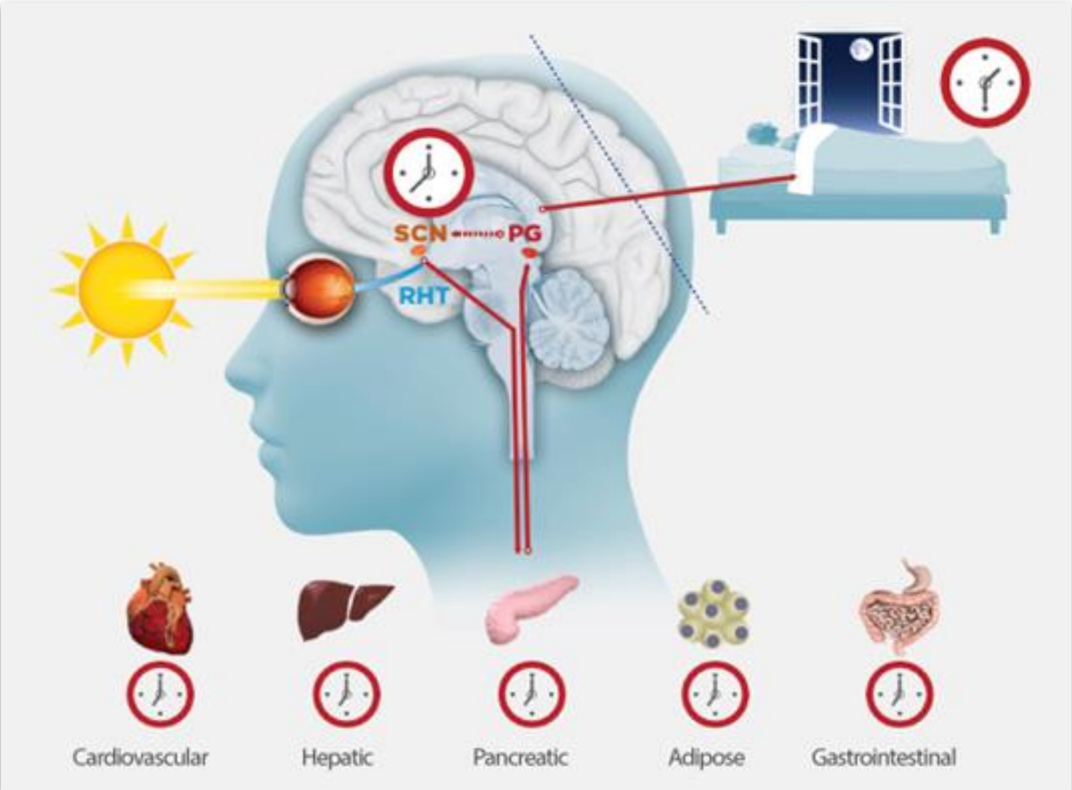
EARLY BIRD

Greater tolerance of morning stress

Body temp rises faster in the am.

Higher cortisol & lower melatonin.

CHRONOTYPES



Genetics

Developmental

NIGHT OWL

Needing calm in the morning

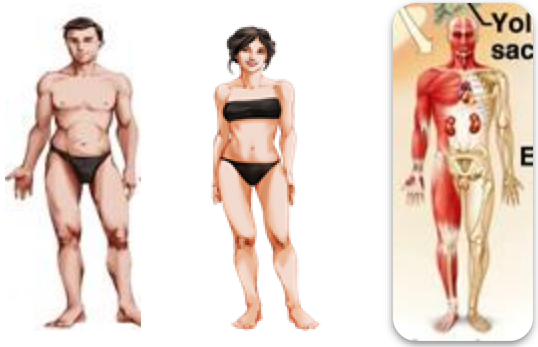
More sensitive to light.

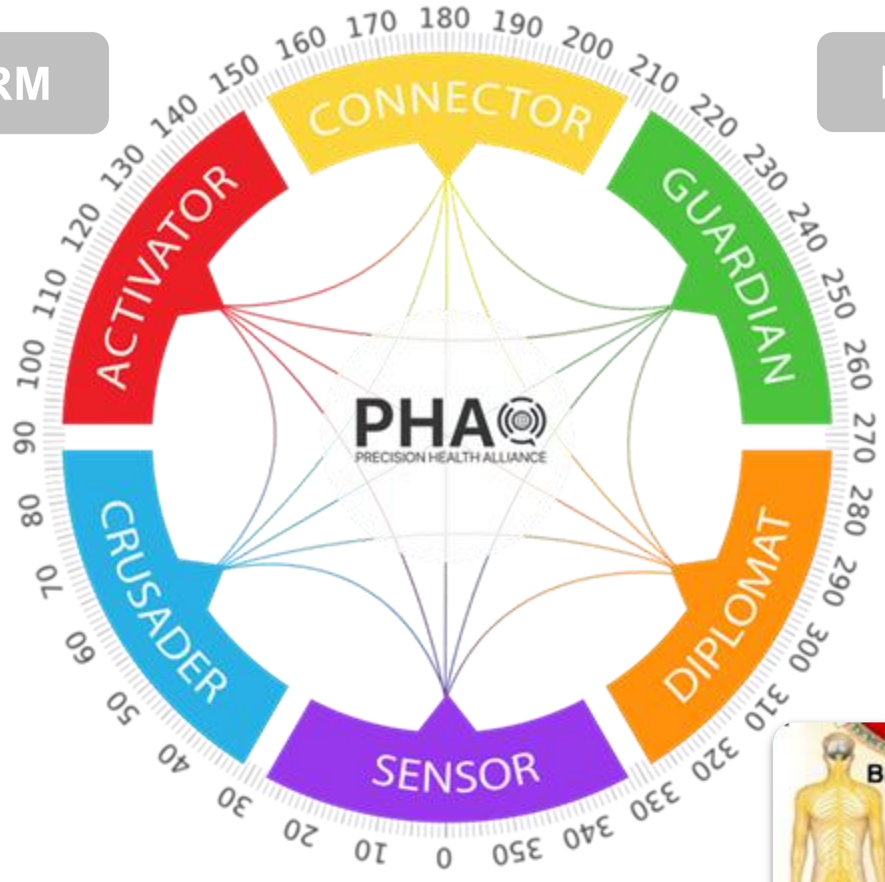
More sensitive to stress in the morning.

PHA PRECISION HEALTH ALLIANCE

Embryo to HealthType

MESODERM





ENDODERM

ECTODERM

Womb environment
determines layer dominance.

Circadian Rhythm & Metabolic Health

Circadian disruptors:

- Artificial light.
- Continual food availability.
- Ever-changing work and social demands on sleep/wake timing.
- Diet and timing of food intake.
- Sleep quality, quantity, and circadian alignment should be considered critical **modifiable factors** in the prevention and management of **insulin resistance**, particularly in **midlife and postmenopausal women**.
- Chronic mild sleep restriction – often overlooked in clinical settings – may constitute a **substantial contributor** to metabolic dysfunction, even in the absence of obesity or overt sleep disorders.

Action Plan for Metabolic Health

- Shelter from ultra-processed foods (Lara Briden)
- Avoid/minimise alcohol, high fructose corn syrup and seed oils
- Higher protein and fibre intake
- Micronutrient balance
- Exercise and maintain muscle mass
- Support mitochondrial health and insulin balance
- Support the gut and microbiome
- Manage luteal phase hormone balance (PMS/PMDD)
- Reconsider certain medications
- Support the autonomic nervous system/vagal nerve tone
- Support circadian alignment and body type rhythms
- Support mental health, dopamine and serotonin levels

Exclusive Live Attendee Resource Giveaway

We very much value your live interaction, questions and comments and would like to thank you for attending!

We have two exclusive resources for live attendees only:

1. Female Metabolic Health Action Plan
2. Nourishing Soups and Smoothies for Female Metabolic Health

These resources will be emailed to you post-webinar.

THANK YOU

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