Circadian rhythm diet

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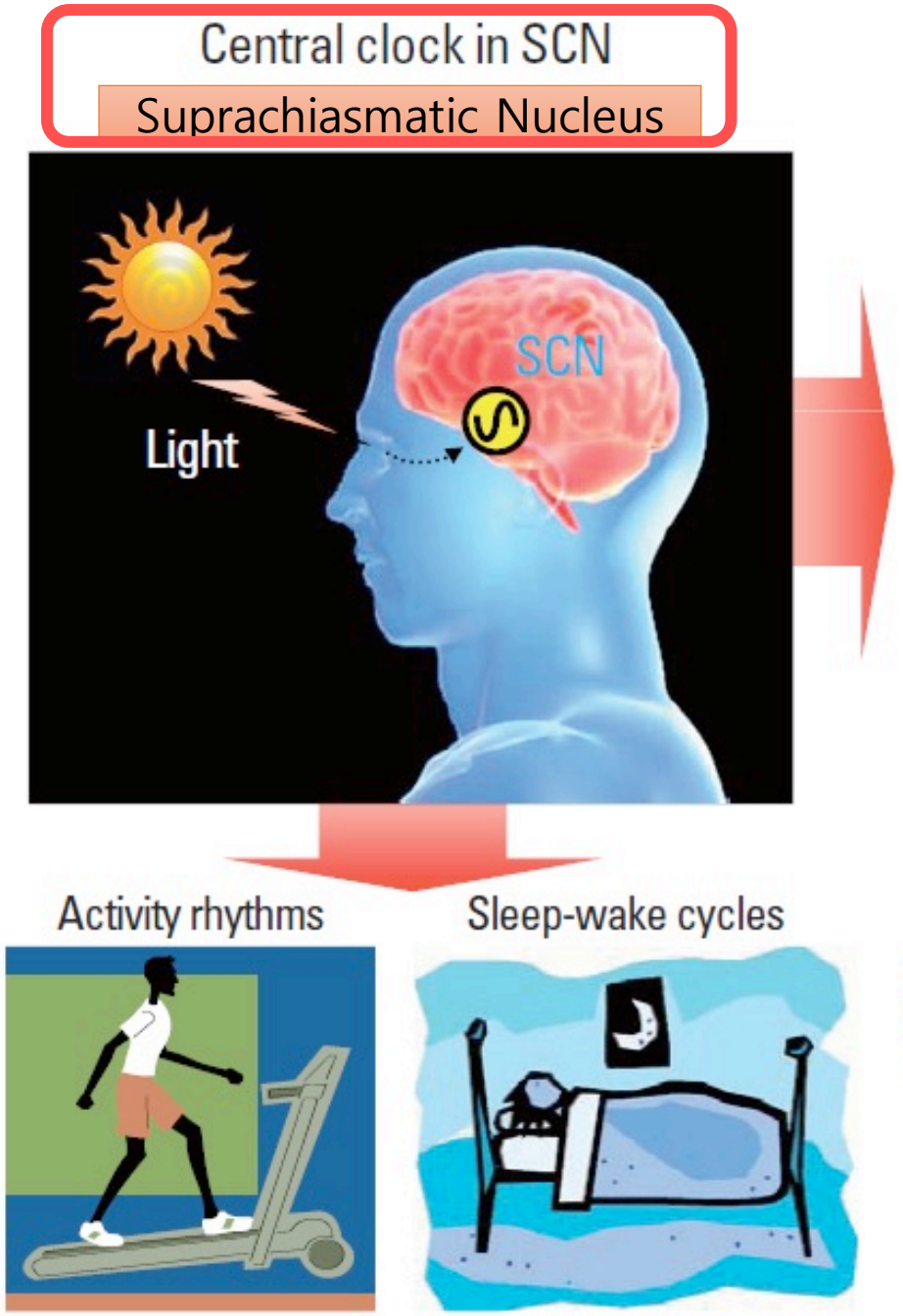
조윤정

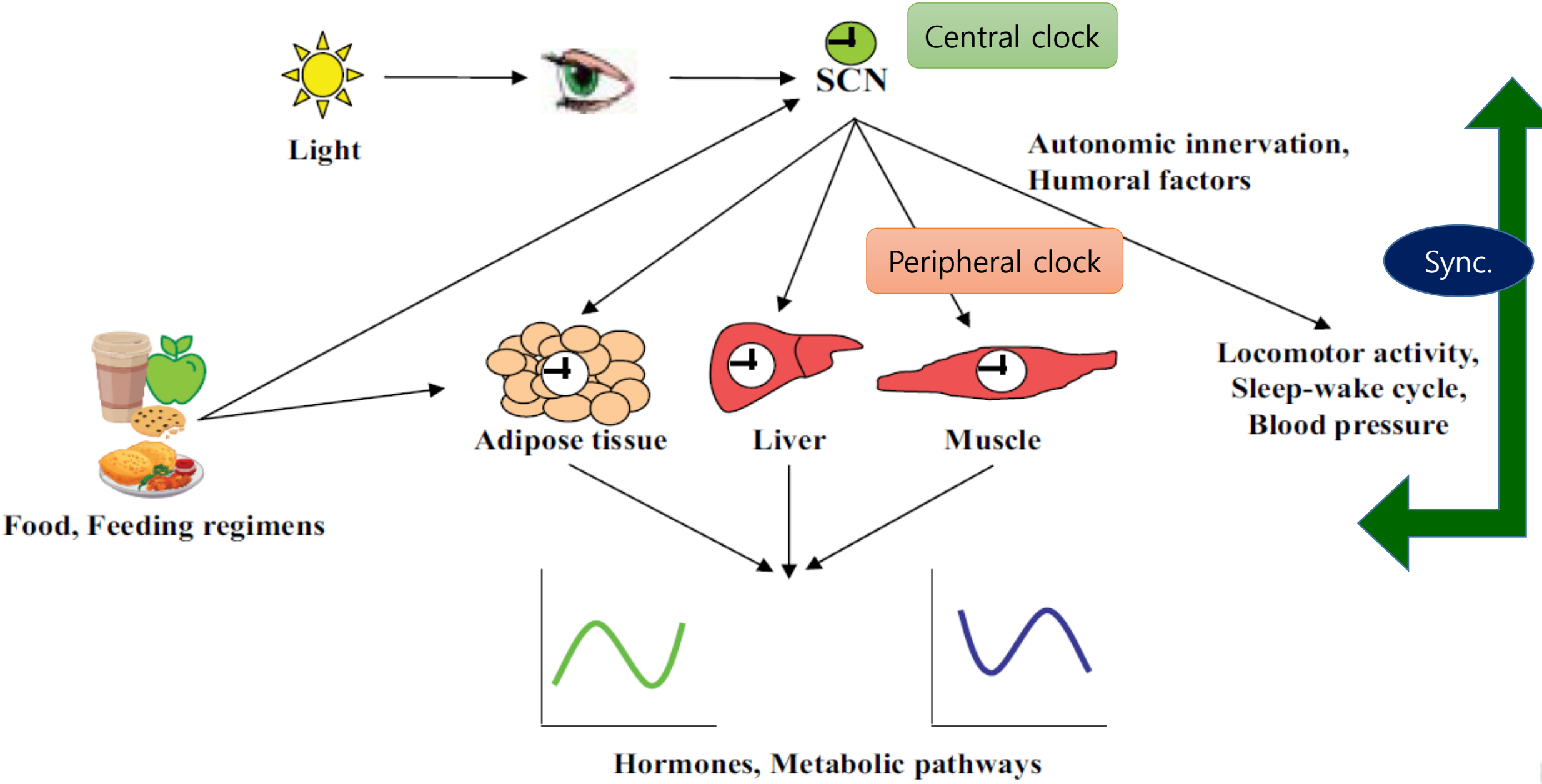
Circadian rhythm

- light and dark cycles 24시간 반복

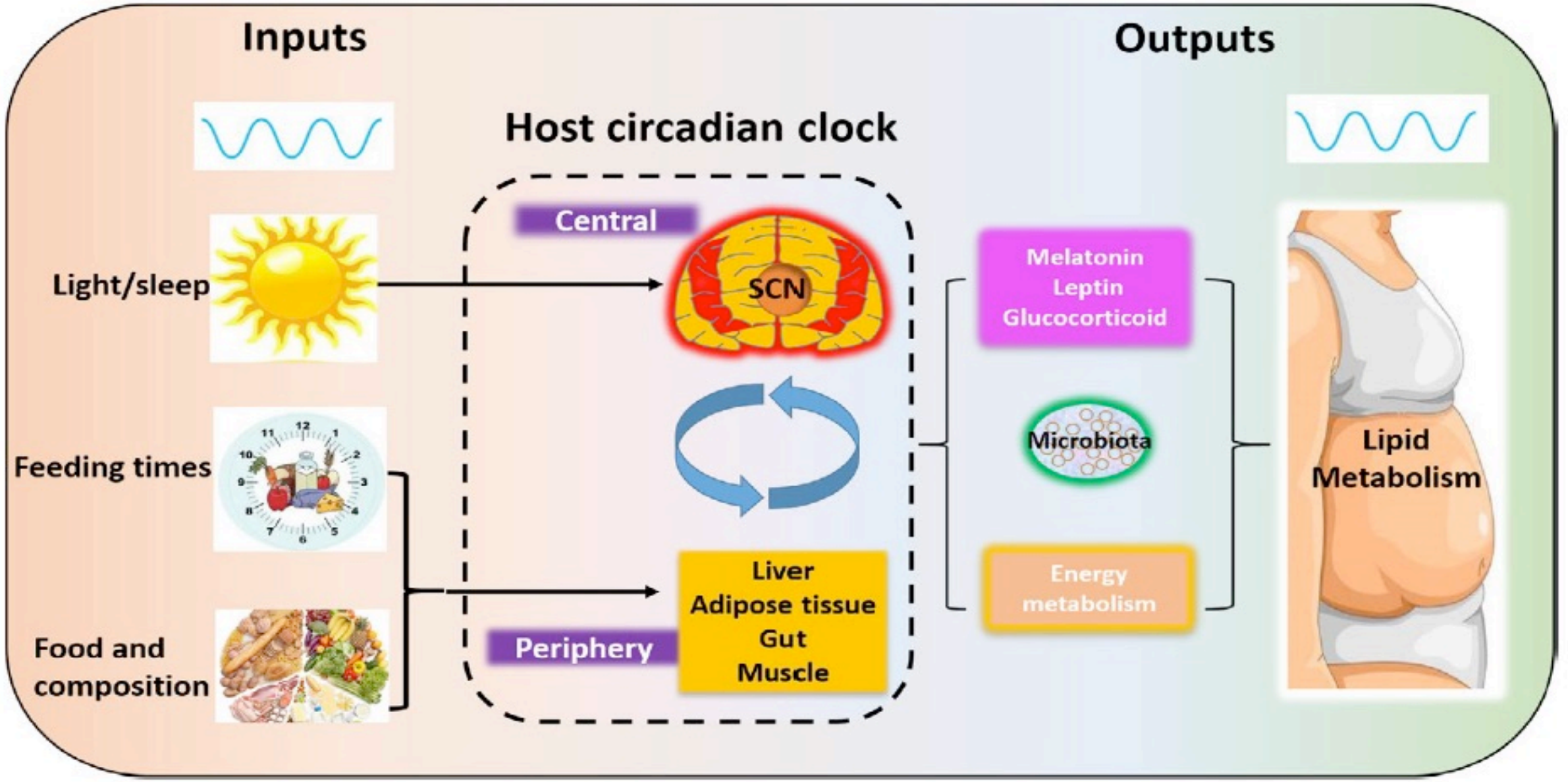
circadian clock.

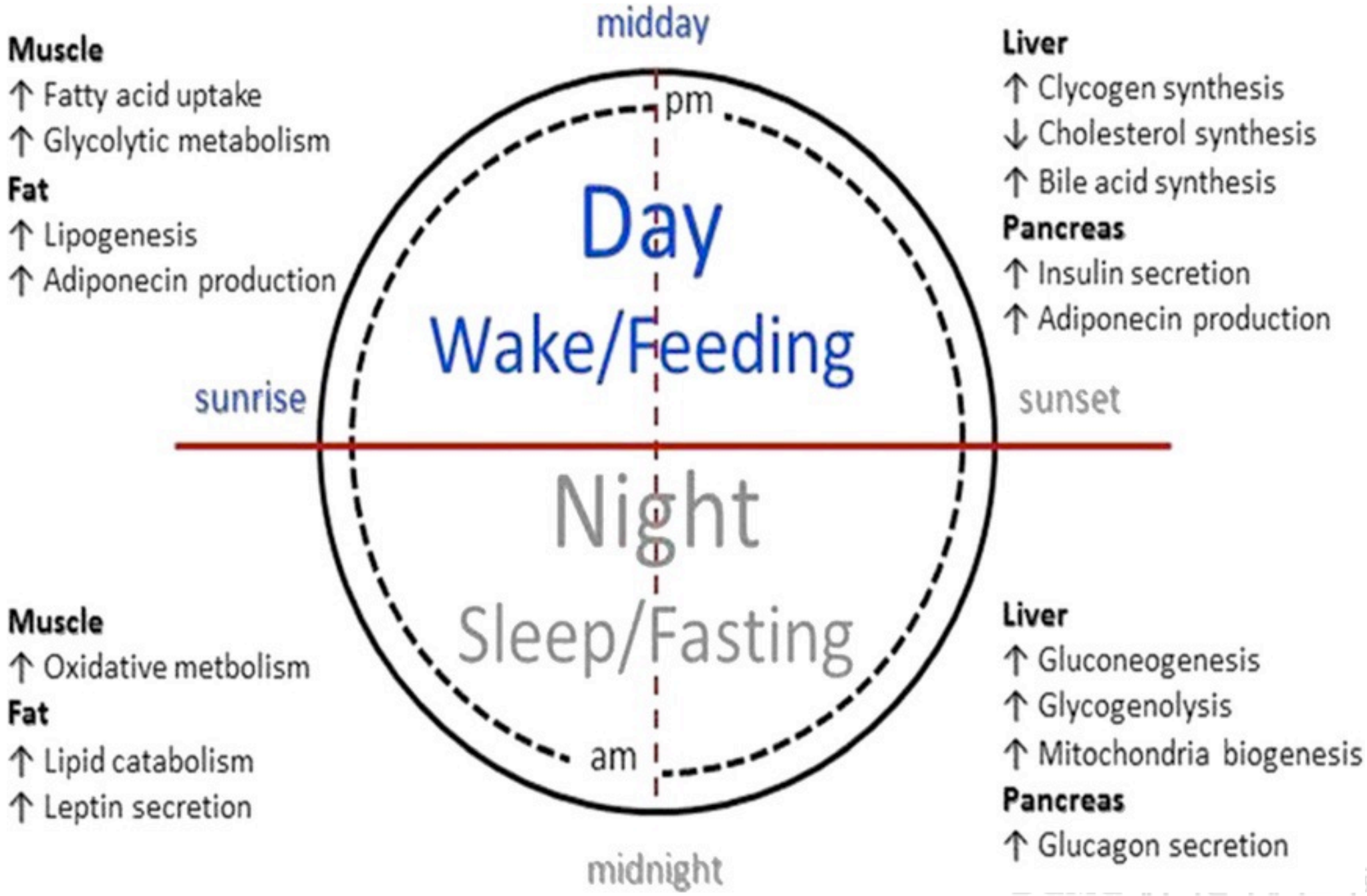
sleep wake cycles, cardiovascular activity, endocrine system, body temperature, renal activity, gastrointestinal tract motility, metabolism (all physiology) 조절에 관여함.



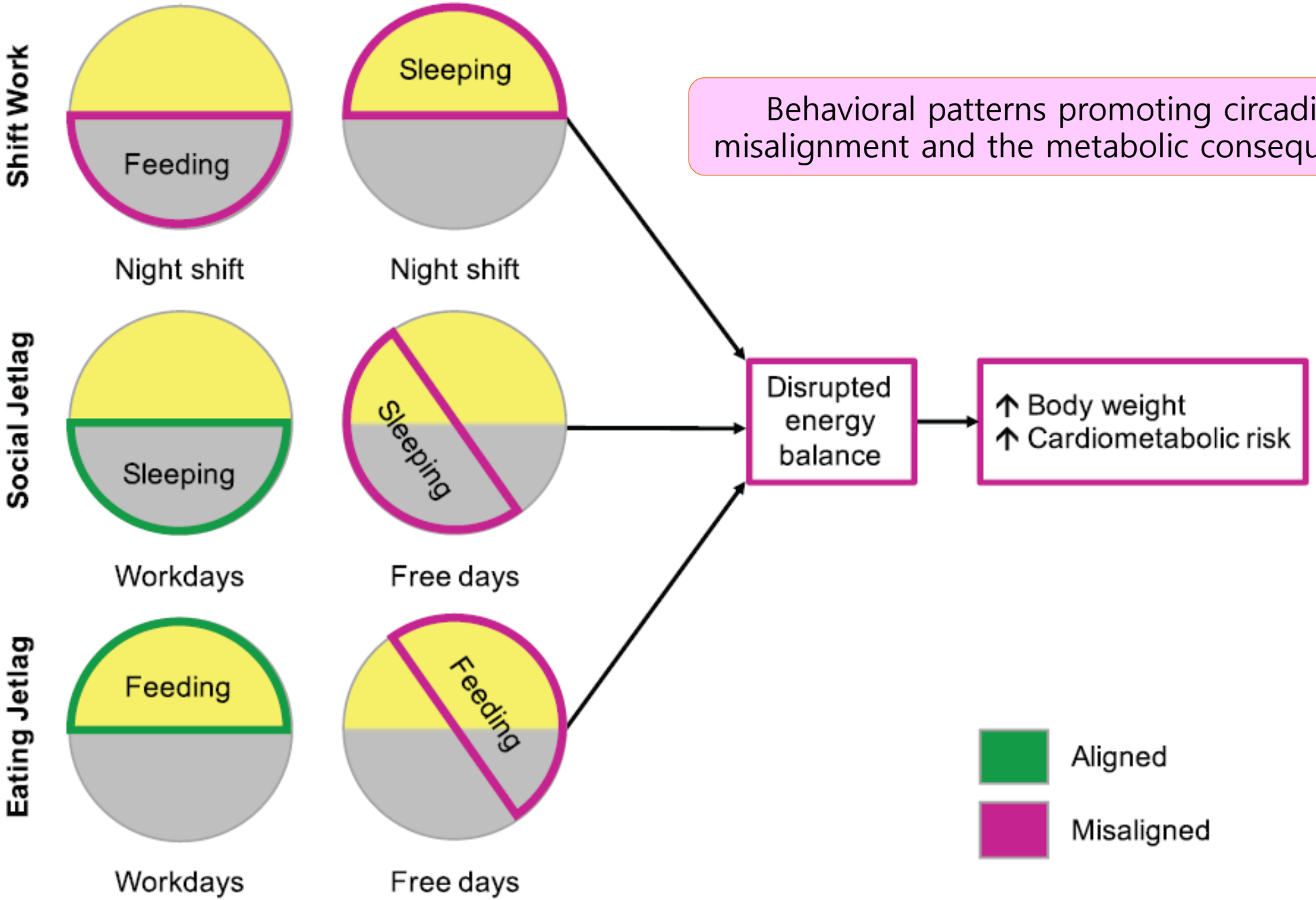

Central clock
SCN
Light
Autonomic innervation,
Humoral factors
Peripheral clock
Sync.
Adipose tissue
Liver
Muscle
Locomotor activity,
Sleep-wake cycle,
Blood pressure
Food, Feeding regimens
Hormones, Metabolic pathways

Systemic signals & coordinators of peripheral oscillators maintaining synchrony of function and health




midday
pm
Day
Wake/Feeding
sunrise
sunset
Night
Sleep/Fasting
am
midnight
Muscle
↑ Fatty acid uptake
↑ Glycolytic metabolism
Fat
↑ Lipogenesis
↑ Adiponecin production
Liver
↑ Clycogen synthesis
↓ Cholesterol synthesis
↑ Bile acid synthesis
Pancreas
↑ Insulin secretion
↑ Adiponecin production
Muscle
↑ Oxidative metbolism
Fat
↑ Lipid catabolism
↑ Leptin secretion
Liver
↑ Gluconeogenesis
↑ Glycogenolysis
↑ Mitochondria biogenesis
Pancreas
↑ Glucagon secretion

Behavioral patterns promoting circadian misalignment and the metabolic consequences

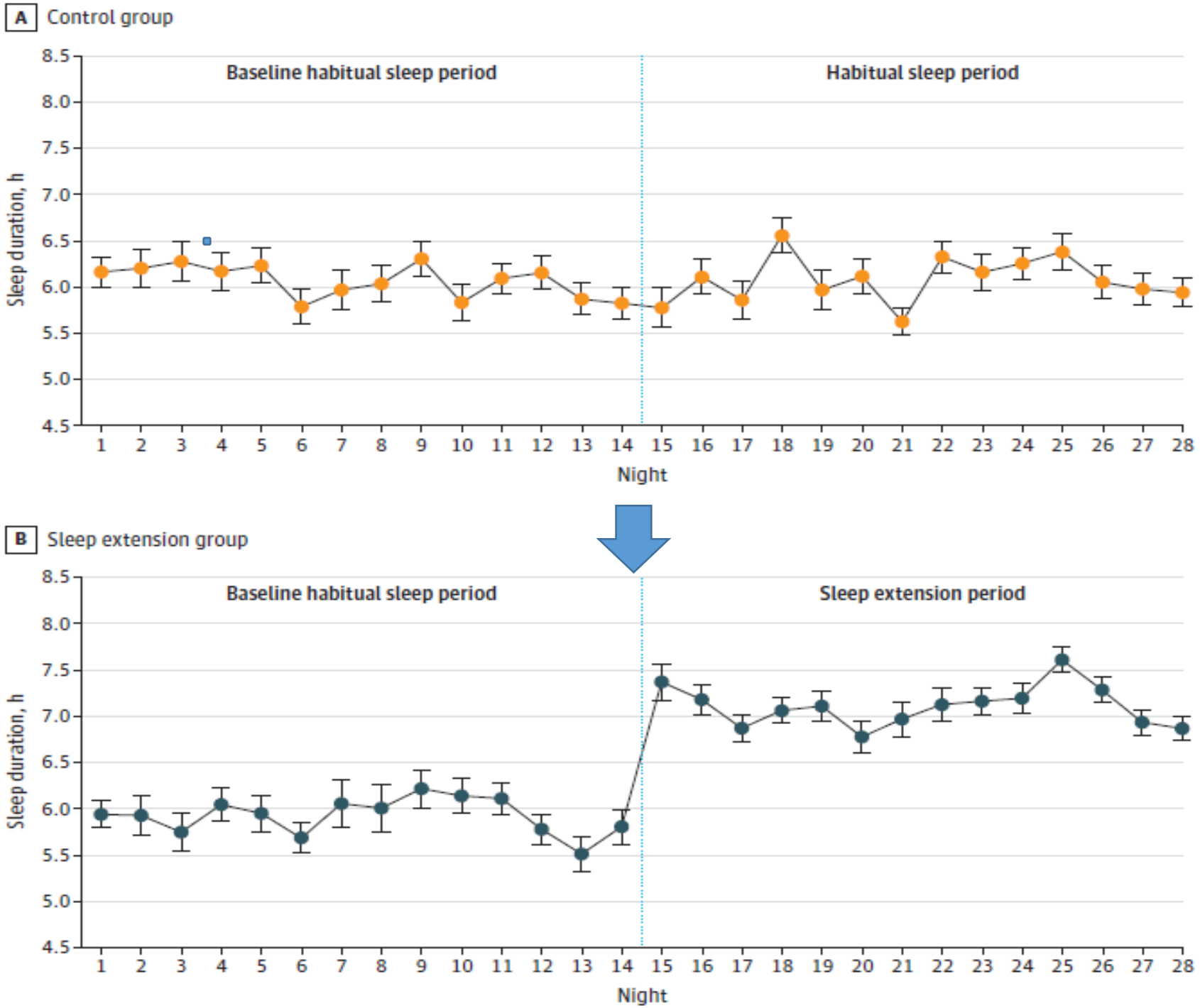


Circadian rhythm, Sleep Extension & Energy Intake

Effect of Sleep Extension on Objectively Assessed Energy Intake Among Adults With Overweight in Real-life Settings A Randomized Clinical Trial.

JAMA Intern Med. doi:10.1001/jamainternmed.2021.8098

- BMI 25.0 -29.9,
  mean [SD] age, 29.8 [5.1] years
- habitual sleep duration:
  6.5시간이하→ 8.5 시간까지
  (sleep extension group)



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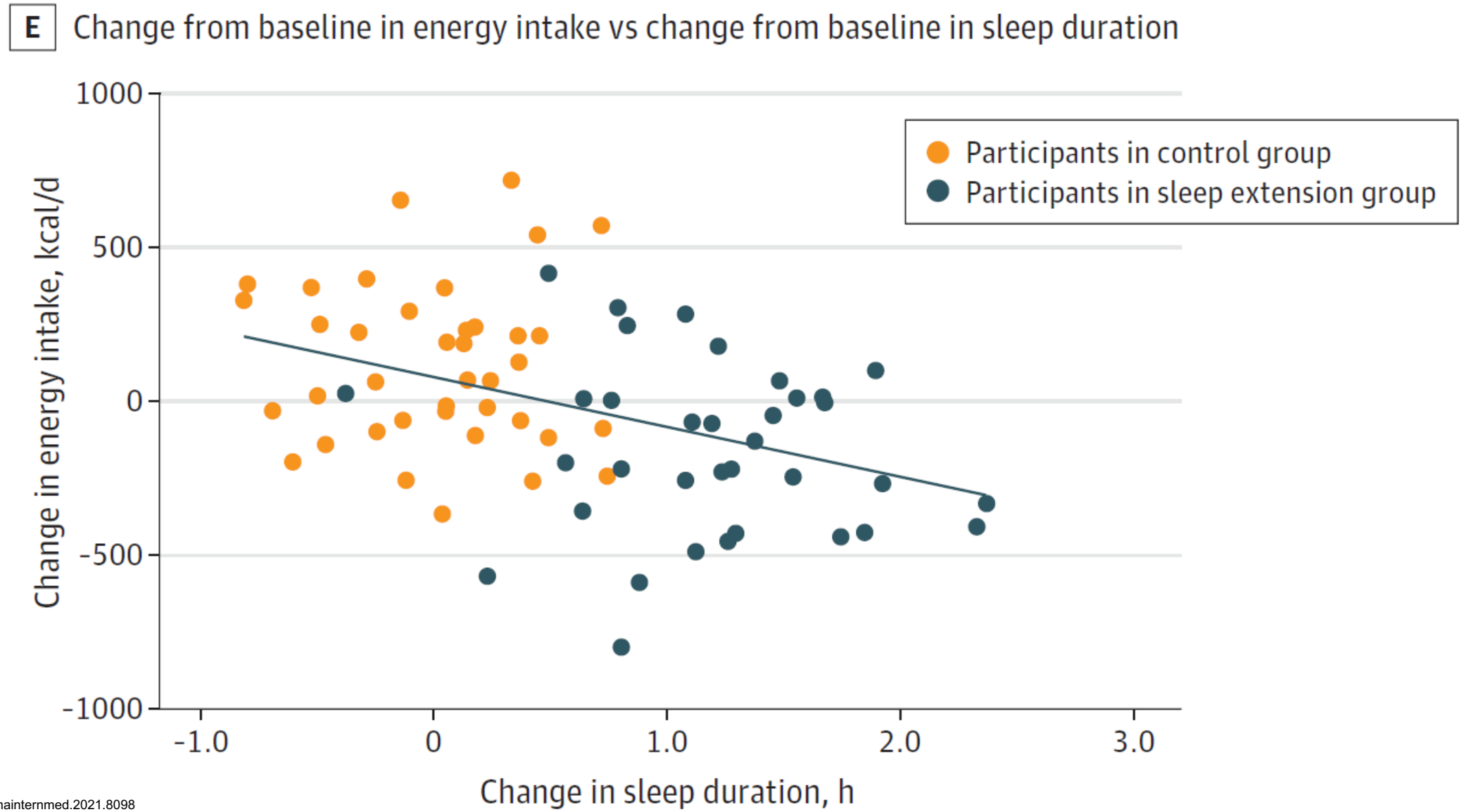
Circadian rhythm, Sleep Extension & Energy Intake



JAMA Intern Med. doi:10.1001/jamainternmed.2021.8098

Effect of Treatment on Energy Intake, Energy Expenditure, and Weight

Variable	Mean (95% CI)							
	Control group (n = 40)			Sleep extension group (n = 40)				
	Baseline habitual sleep	Habitual sleep	Change from baseline	Baseline habitual sleep	Sleep extension	Change from baseline	Differences in changes (95% CI)	*P* value
Energy intake, kcal/d	2665.0 (2468.4 to 2861.6)	2779.9 (2583.3 to 2976.5)	114.9 (29.6 to 200.2)	2976.6 (2782.5 to 3170.7)	2821.1 (2625.1 to 3017.2)	−155.5 (−244.1 to −66.9)	−270.4 (−393.4 to −147.4)	<.001
Total energy expenditure, kcal/d	2693.5 (2499.9 to 2887.1)	2700.7 (2507.1 to 2894.3)	7.2 (−49.0 to 63.3)	2871.1 (2677.6 to 3064.7)	2824.4 (2630.2 to 3018.6)	−46.7 (−105.1 to 11.6)	−53.9 (−134.9 to 27.1)	.19
Energy balance, kcal/d	−0.6 (−69.9 to 68.8)	105.4 (36.0 to 174.8)	106.0 (19.0 to 193.0)	105.4 (36.9 to 174.0)	0.4 (−71.7 to 72.4)	−105.1 (−193.8 to −16.3)	−211.1 (−335.4 to −86.8)	.001
Resting metabolic rate, kcal/d								
Fasting	1563.6 (1487.3 to 1640.0)	1581.1 (1504.5 to 1657.6)	17.4 (−4.9 to 39.7)	1667.8 (1591.3 to 1744.2)	1652.7 (1576.2 to 1729.3)	−15.1 (−38.0 to 7.9)	−32.5 (−64.5 to −0.5)	.047
Postprandial	1837.9 (1746.6 to 1929.2)	1859.7 (1768.0 to 1951.4)	21.8 (−6.5 to 50.1)	1944.9 (1853.4 to 2036.5)	1949.8 (1858.1 to 2041.4)	4.8 (−24.2 to 33.9)	−17.0 (−57.5 to 23.6)	.41
Thermic effect of meal, kcal[b]	45.7 (41.4 to 50.1)	46.6 (42.2 to 51.1)	0.9 (−3.2 to 5.0)	46.3 (41.9 to 50.8)	49.1 (44.6 to 53.6)	2.8 (−1.5 to 7.0)	1.8 (−4.0 to 7.7)	.54
Activity energy expenditure, kcal/d	878.9 (759.7 to 998.0)	863.7 (743.2 to 984.1)	−15.2 (−81.0 to 50.5)	951.2 (832.8 to 1069.7)	918.1 (798.8 to 1037.5)	−33.1 (−100.5 to 34.3)	−17.9 (−112.1 to 76.3)	.71
Weight change, kg[c]	−0.04 (−0.33 to 0.25)	0.35 (0.06 to 0.64)	0.39 (0.02 to 0.76)	0.45 (0.16 to 0.73)	−0.03 (−0.33 to 0.27)	−0.48 (−0.85 to −0.11)	−0.87 (−1.39 to −0.35)	.001
Fat-free mass change, kg	−0.05 (−0.27 to 0.17)	0.22 (−0.003 to 0.44)	0.26 (−0.01 to 0.54)	0.32 (0.11 to 0.54)	−0.03 (−0.26 to 0.19)	−0.36 (−0.64 to −0.08)	−0.62 (−1.02 to −0.23)	.002
Fat mass change, kg	0.004 (−0.08 to 0.09)	0.13 (0.05 to 0.21)	0.13 (0.03 to 0.23)	0.12 (0.04 to 0.20)	−0.00 (−0.08 to 0.08)	−0.12 (−0.22 to −0.02)	−0.25 (−0.39 to −0.10)	.001

JAMA Intern Med. doi:10.1001/jamainternmed.2021.8098

식사요법 for Obesity

체중 감량 목표 설정

목표 체중 도달을 위한 에너지 섭취량 결정

영양소 비율과 배분

적절한 식품 종류, 양 결정

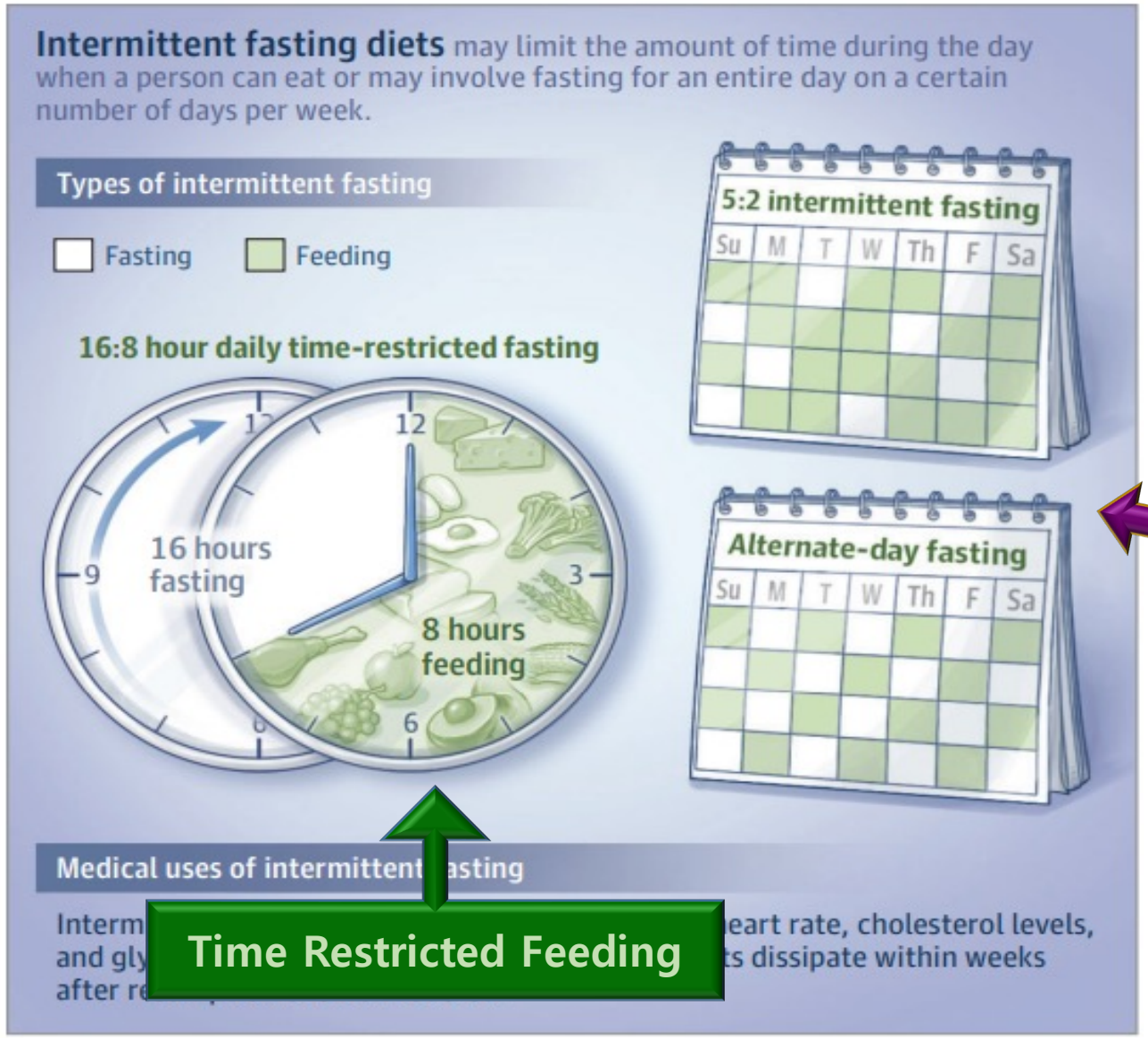
식단 구성

Diet strategies for weight control

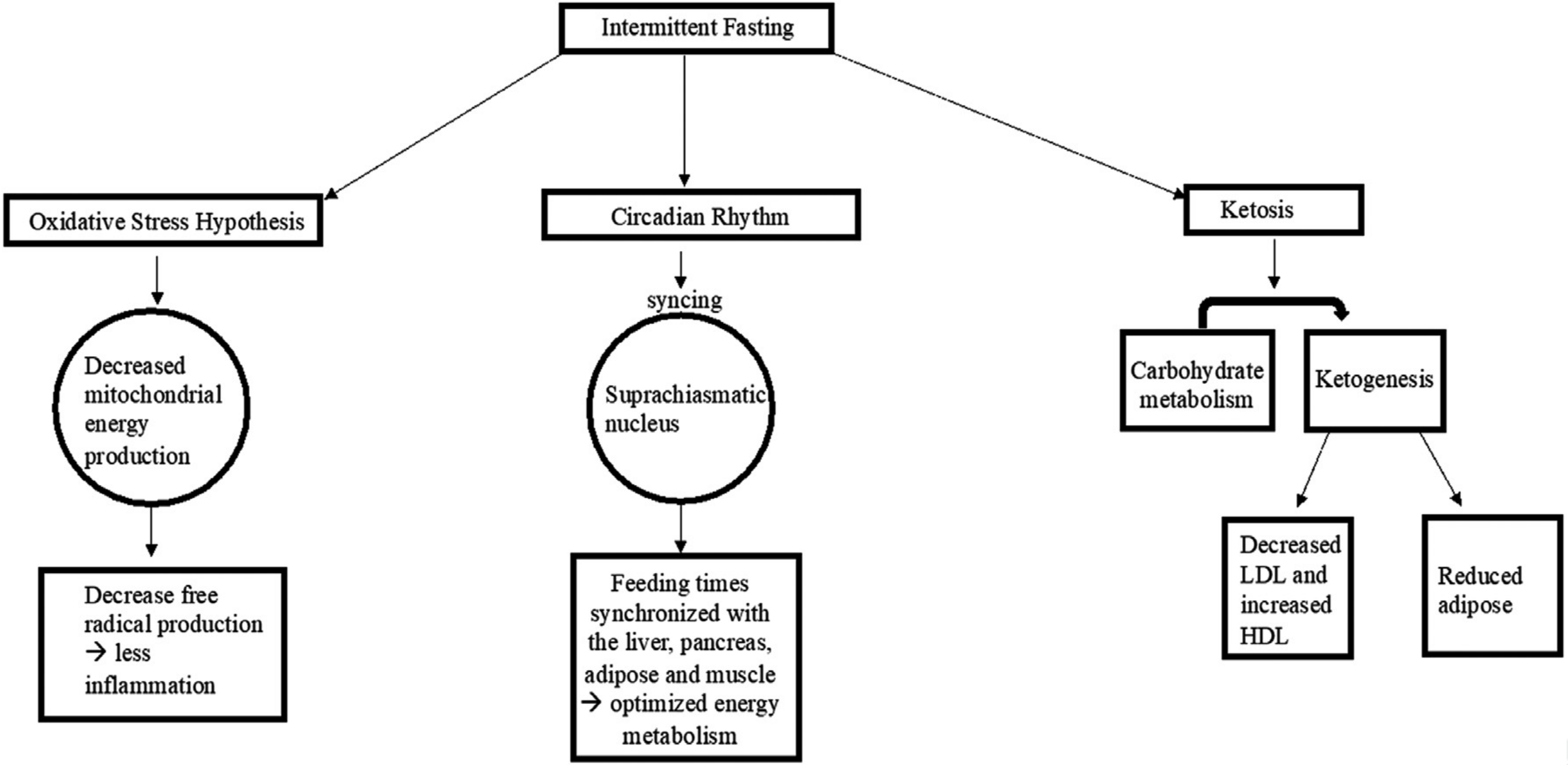
- Traditional Comprehensive lifestyle intervention for obesity management
  - **Continuous energy restriction** // and its limitation
  - Various weight-loss diets

- Alternative Strategies for Weight Control
  - Fasting
  - Meal timing/ Eating frequency
  - Intermittent energy restriction
  - **Intermittent fasting**: focuses on the timing of when one can consume meals either within a day or a week

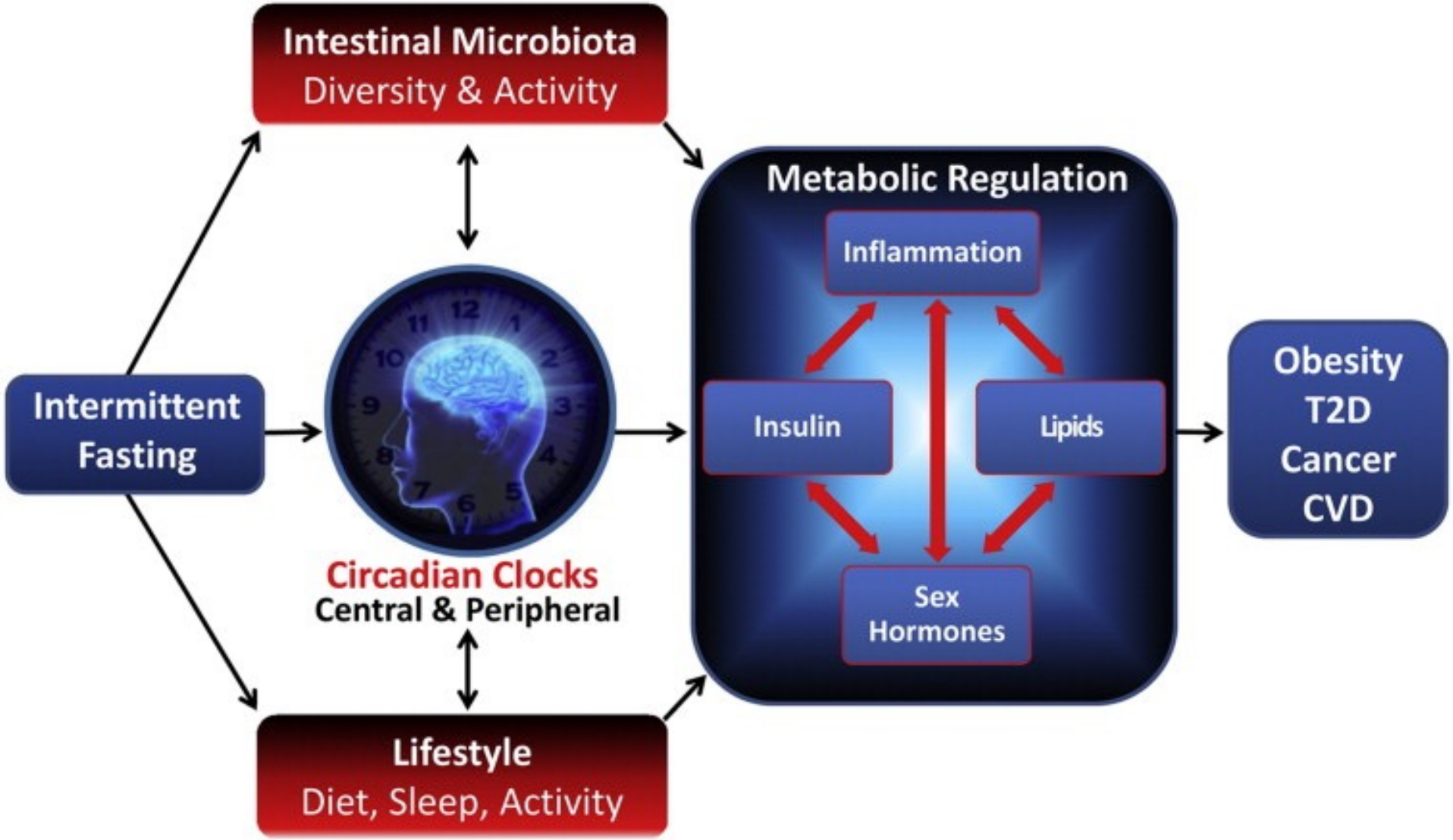
간헐적 단식



Intermittent fasting
(Alternate day fasting..)

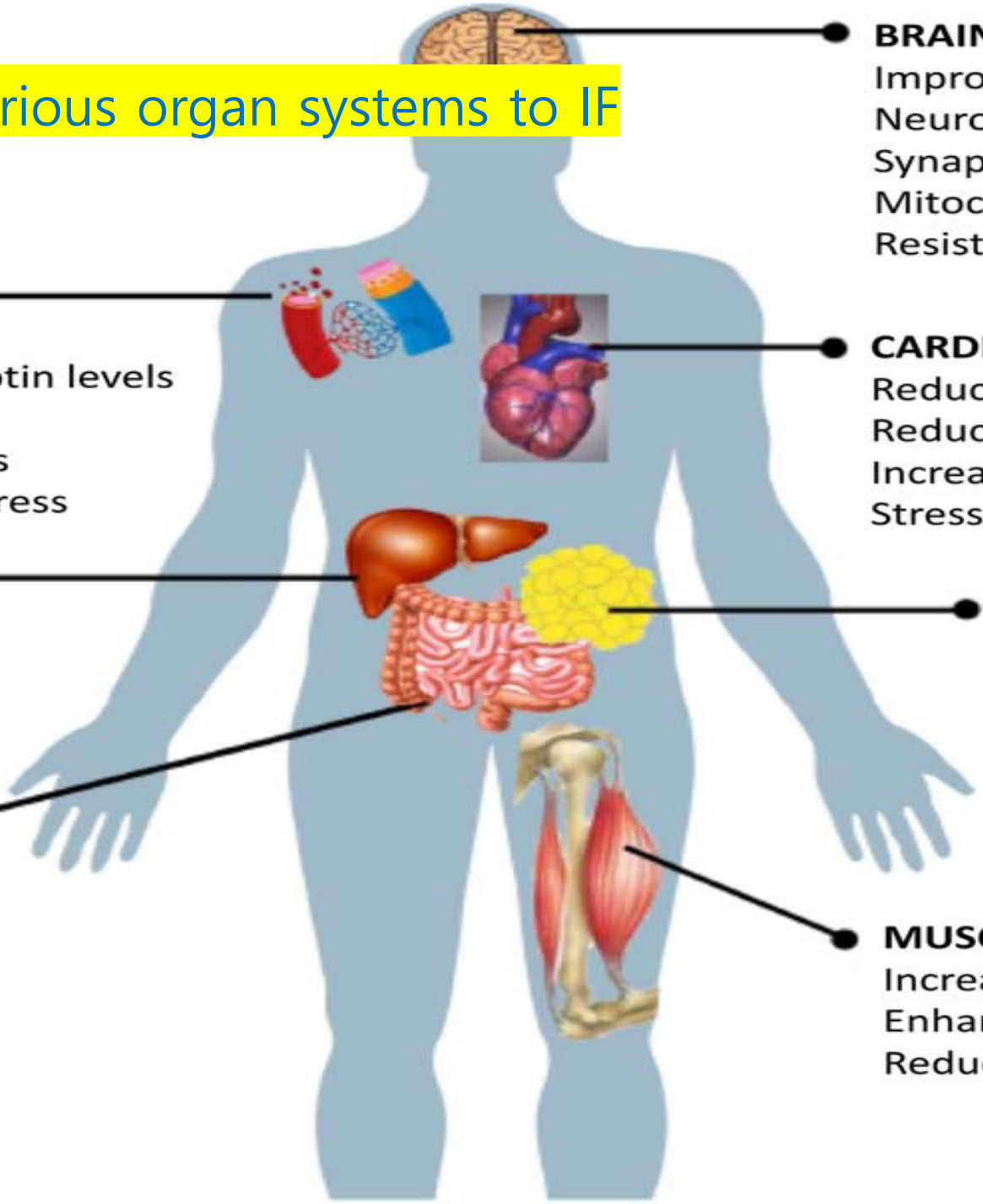

Intermittent Fasting
Oxidative Stress Hypothesis
Circadian Rhythm
Ketosis
Decreased mitochondrial energy production
Decrease free radical production → less inflammation
syncing
Suprachiasmatic nucleus
Feeding times synchronized with the liver, pancreas, adipose and muscle → optimized energy metabolism
Carbohydrate metabolism
Ketogenesis
Decreased LDL and increased HDL
Reduced adipose

Intermittent fasting & Metabolic regulation



J. Acad. Nutr. Diet. 115:1203–12
Annu. Rev. Nutr. 2017. 37:371–93

Functional effects of various organ systems to IF



BRAIN
Improved cognition
Neurotrophic factor production*
Synaptic plasticity*
Mitochondrial biogenesis*
Resistance to injury and disease*

BLOOD
Elevated ketone levels
Reduced glucose, insulin and leptin levels
Elevated adiponectin levels
Reduced inflammatory cytokines
Reduced markers of oxidative stress

CARDIOVASCULAR SYSTEM
Reduced blood pressure
Reduced resting heart rate
Increased parasympathetic tone
Stress resistance*

LIVER
Glycogen depletion
Ketone production
Increased insulin sensitivity
Reduced lipid accumulation

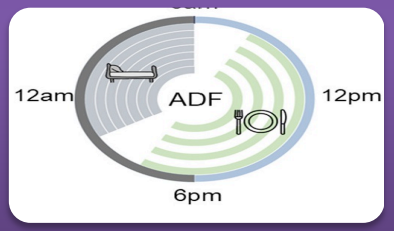
ADIPOSE TISSUE
Lipolysis
Reduced leptin production
Reduced inflammation

INTESTINES
Enhanced motility
Reduced inflammation

MUSCLE
Increased insulin sensitivity
Enhanced efficiency/endurance
Reduced inflammation

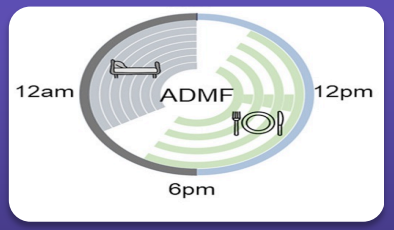
Obesity (2018) 26, 254-268.

Different Types of Intermittent fasting



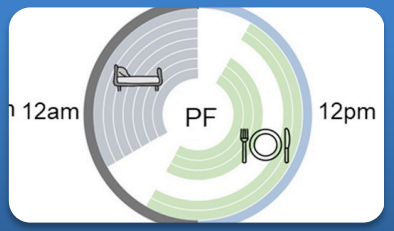
Alternate-day fasting (ADF)

- consuming no calories on fasting days and alternating fasting days with a day of unrestricted food intake, or a "feast" day (zero calorie intake on fast days)



Modified Alternate-day fasting (MADF)

- consuming less than 25% of baseline energy needs on "fasting" days, alternated with a day of unrestricted food intake, or a "feast" day.



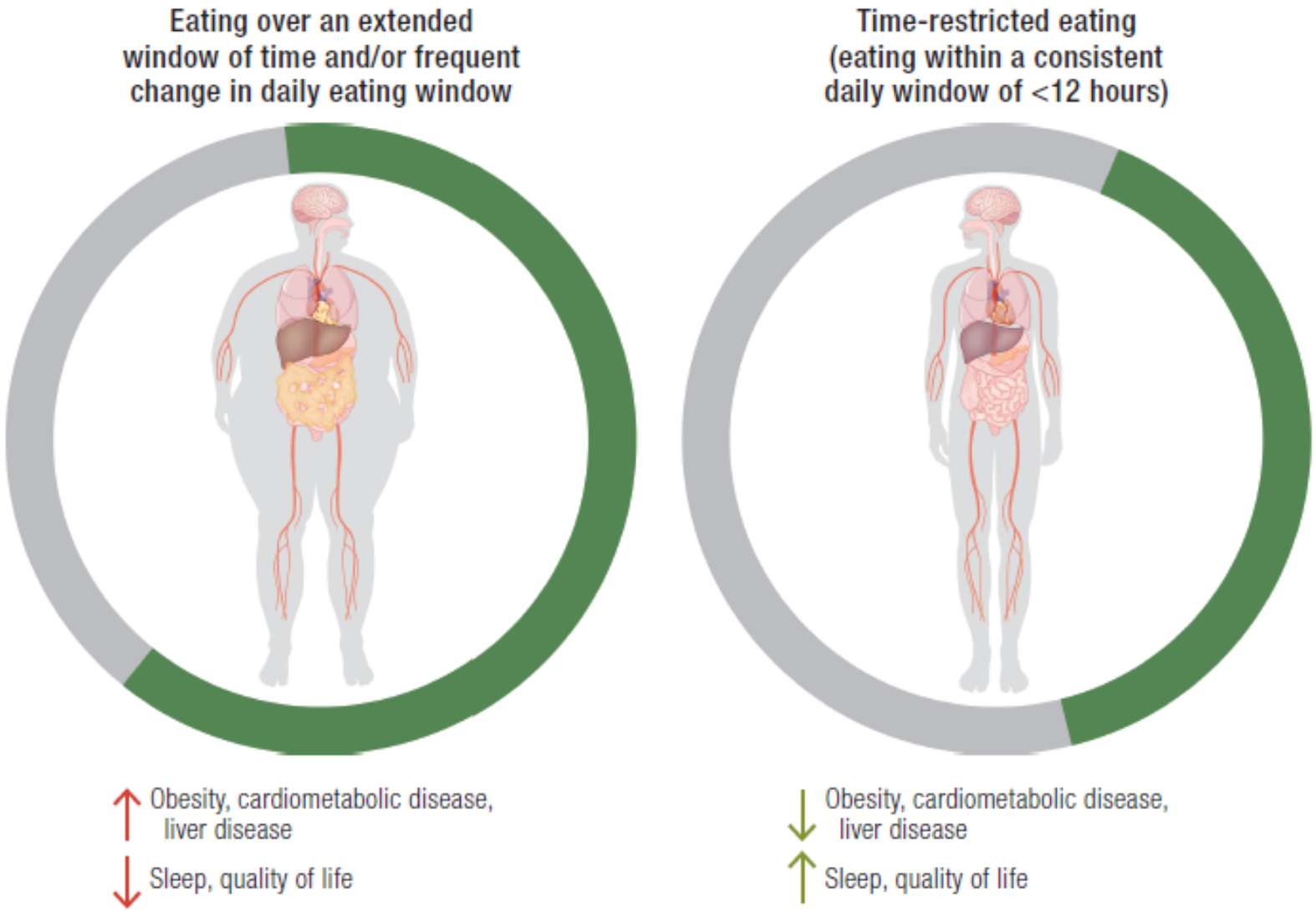
Periodic fasting(PF)

- fasting only 1-2 d/wk and consuming food ad libitum on 5-6 d/wk

Time-restricted feeding /eating (TRF/TRE)

- **restricting food intake to specific time periods of the day, typically between 8 and 12 h each day.**

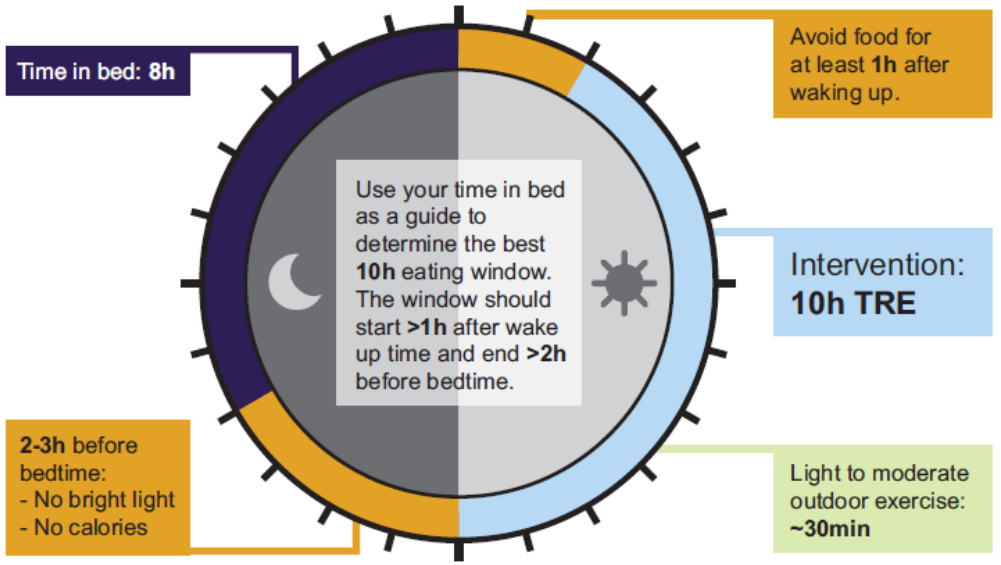
Timing of food intake and human health



Various approaches to time-restricted eating (TRE)

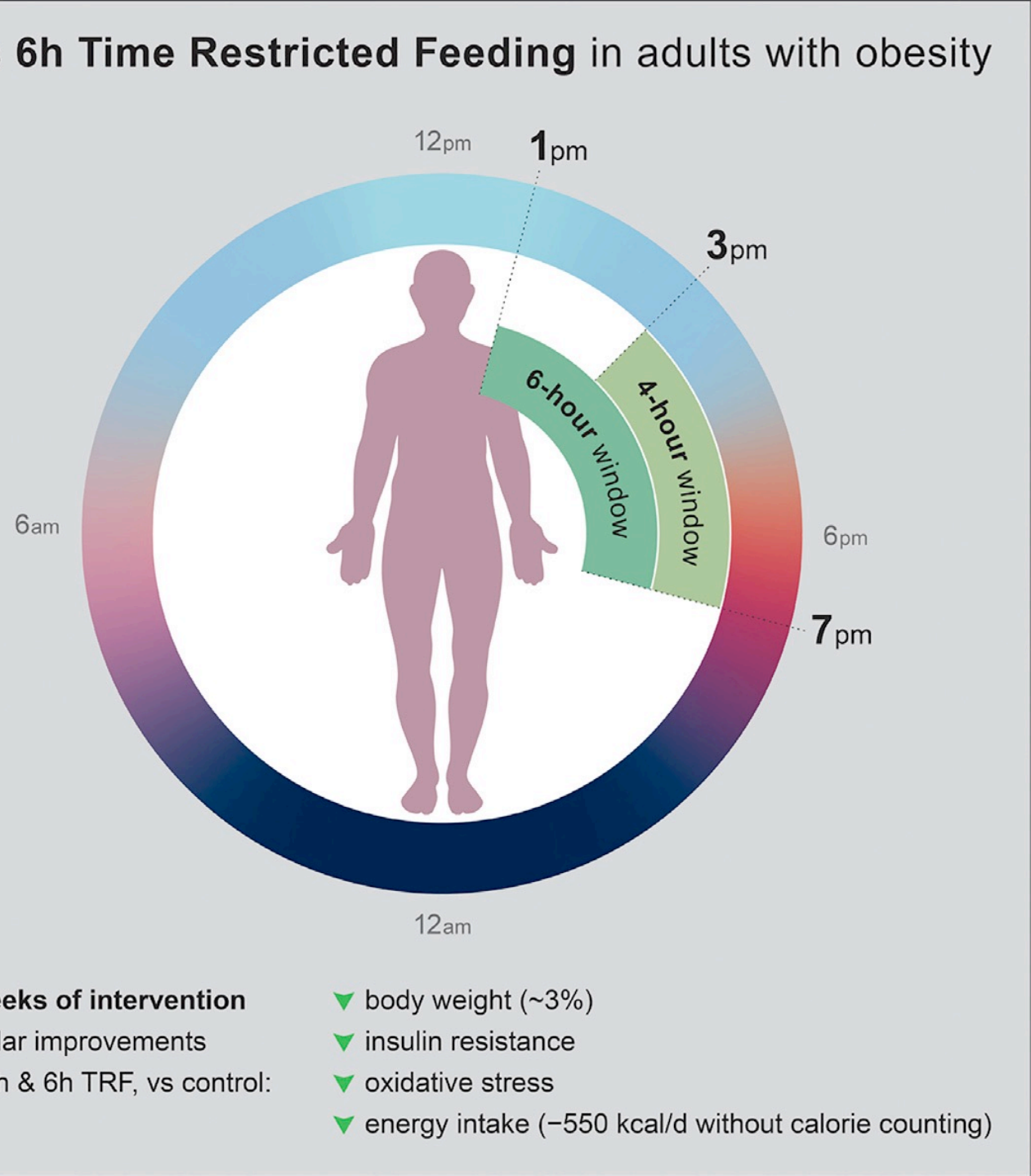
- **the window of time** : eating vs. fasting
- Eating time 의 일관성이 필요함.

- TRF models in rodents and flies
  - 8- to 12-hour eating windows → 전반적으로 긍적적 효과.
  - greater results?, 8- to 9-hour eating windows
- Clinical trials on TRE in humans
  - typically choose 8- to 10-hour.
  - 4 or 6 hours ~~ 12 hours
  - ongoing clinical trials

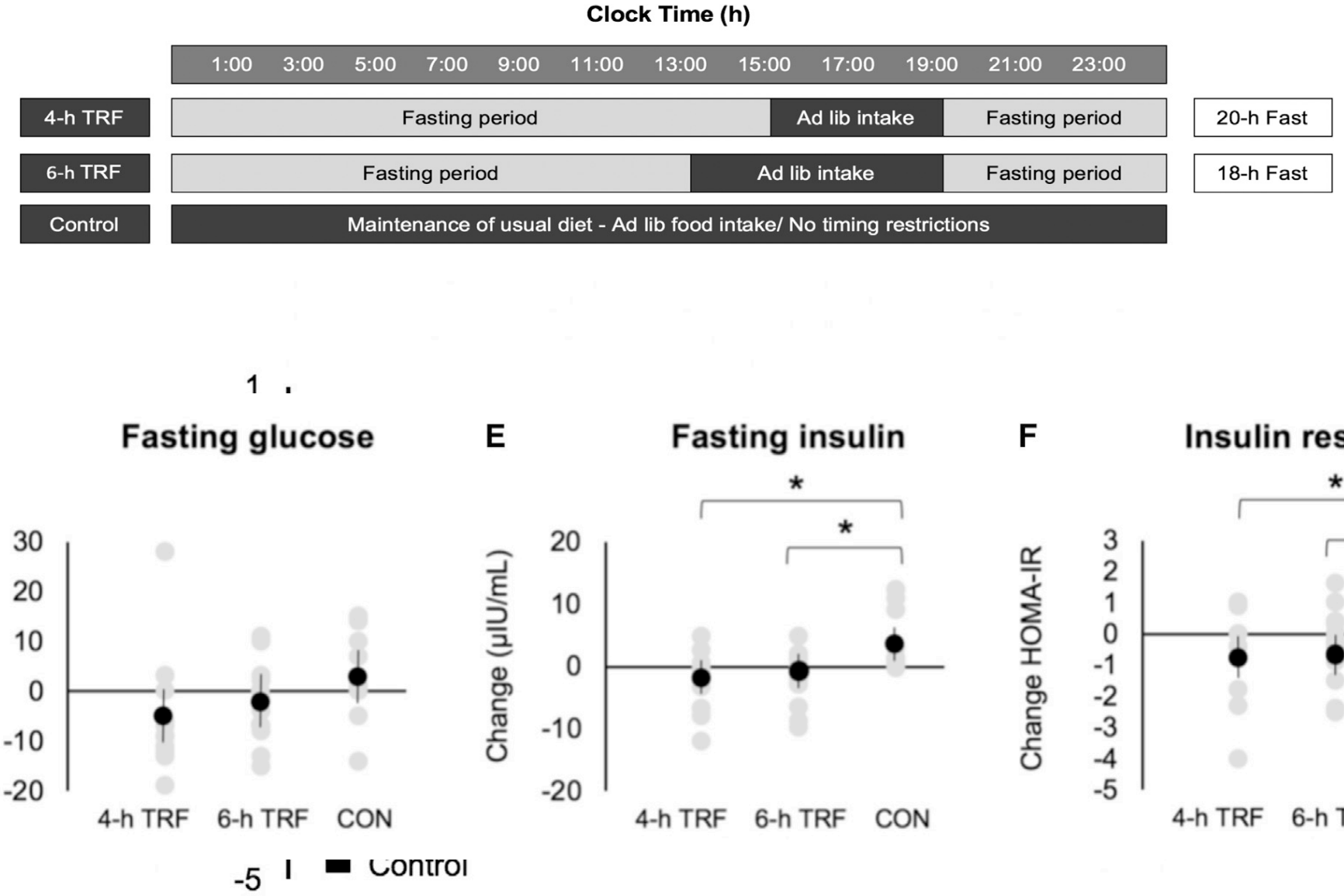


Effects of 4- and 6-h Time-Restricted Feeding on Weight and Cardiometabolic Health: A Randomized Controlled Trial in Adults with Obesity

- Adults in obesity, 2mon
- 4- vs. 6-h time-restricted feeding
- 양군 모두 E. intake 줄임.

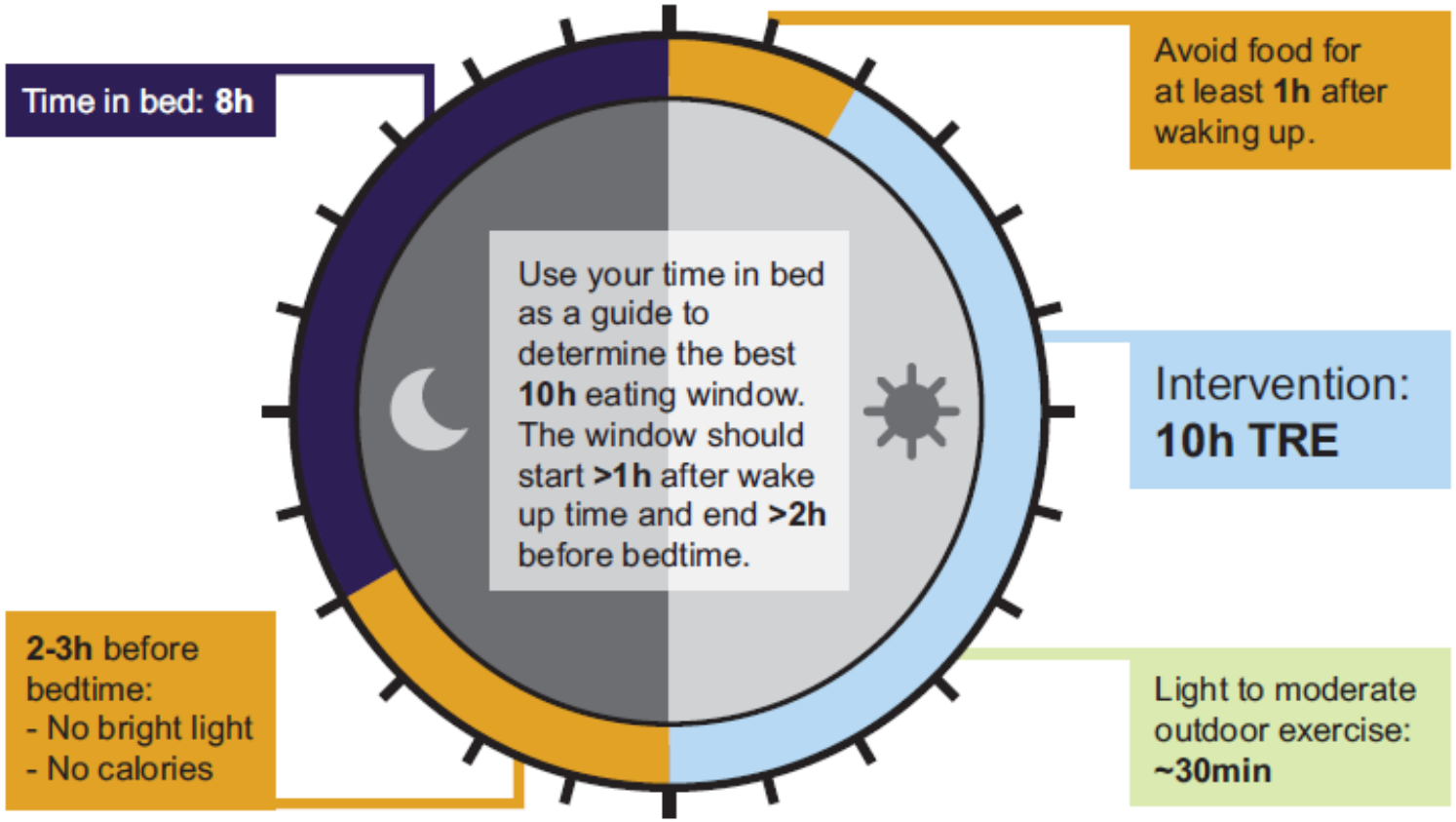


Cell Metabolism 32, 366–378



- similar reductions in weight, insulin resistance and oxidative stress

Time restricted eating (TRE) intervention



Duration.

- 6- & 10-hour eating window >> 12-hour
- 10-hour eating window ≒↔6~8 hours

- 6 hours or less

: mild adverse side effects (ex. Headache)

- eating window: 8 ~10 hours

:순응도, 원할할 진행을 위해 계획해볼 수 있는 eating window

Phase

수면과 대사에서의 circadian rhythms을 고려하여 접근.
Melatonin 분비 고려.

some research: eating in the earlier phase of the day >> delayed eating

Time restricted eating (TRE) intervention

- TRE의 Clinical trials는 2013 ~ 2015에 시작. 거대하게 증가하였고 현재도 많은 연구들이 진행중임.
- **연구대상자**:

  lean and healthy adults, overweight, and obese subjects (가장 많음), metabolic disturbances(예, prediabetes, type 2 diabetes, metabolic syndrome, or NAFLD...
- type 2 diabetes 연구에서는 중재가 복잡하였음.* 저혈당
- Mostly short-term trials (4 days to 12 weeks), relatively small number of subjects (8 to 80 participants)

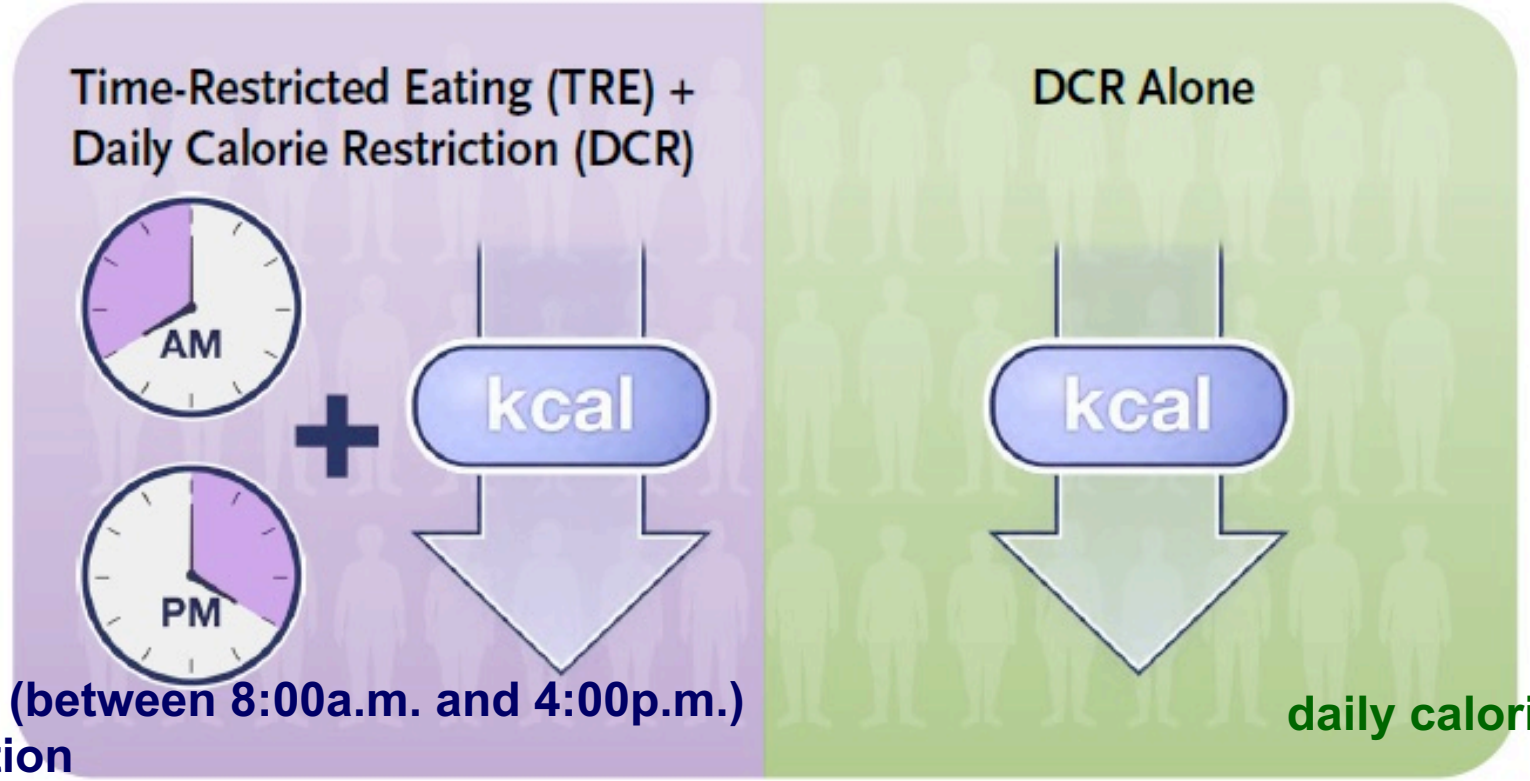
- **TRE의 적용이 부적절한 그룹**

  e.g., children & teenagers (actively growing), taking drugs or insulin injections (특히type 1 diabetes), acute illness, eating disorders, pregnancy, breastfeeding, severe kidney and liver diseases, cancer.

- TRE 의 효과에 대한 확인?

Calorie Restriction with or without Time-Restricted Eating in Weight Loss

BMI: 28 ~ 45
Calory intake: 1500-1800 kcal/day (for men), 1200-1500 kcal/day (for women)
12-month follow-up



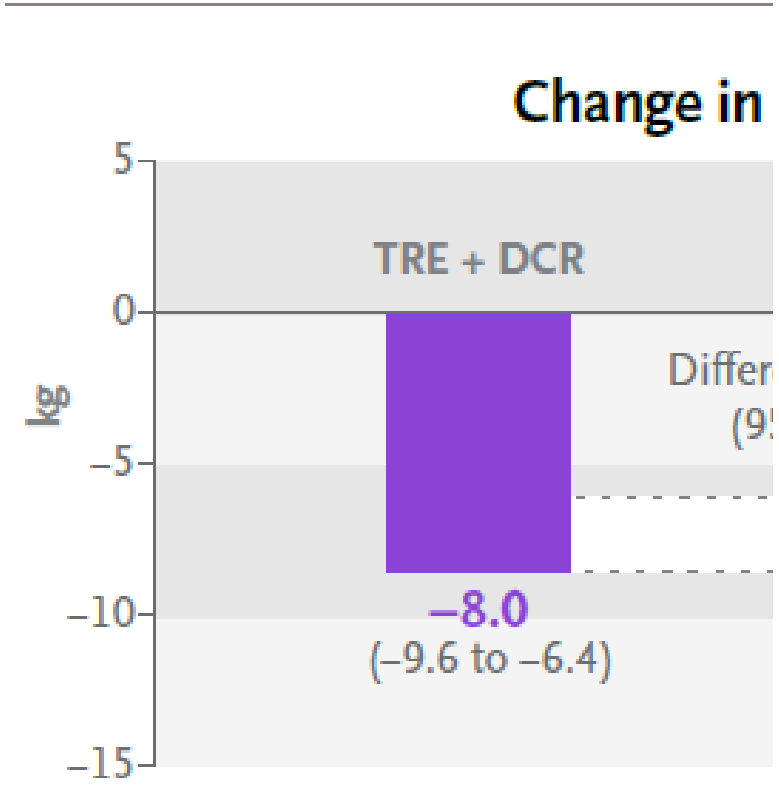
time-restricted eating (between 8:00a.m. and 4:00p.m.) + daily calorie restriction

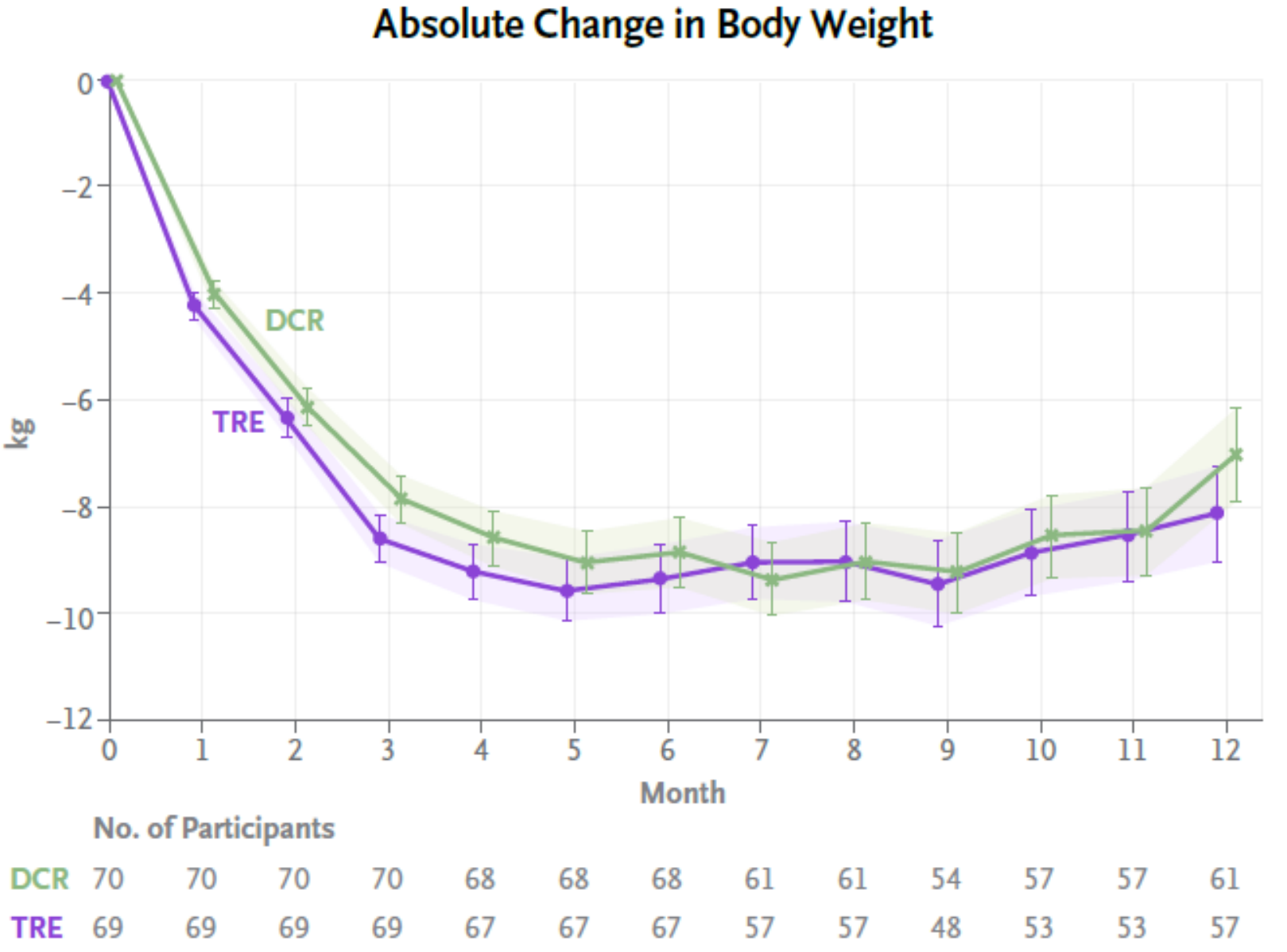
daily calorie restriction alone

Time-Restricted Eating (N = 69)

Daily Calorie Restriction (N = 70)

Calorie Restriction with or without Time-Restricted Eating in Weight Loss





N Engl J Med 2022;386:1495-504.

Time restricted eating (TRE) intervention

향후 TRE 의 효과를 확인하기위하여..

(1) carefully monitoring macronutrient and calorie intake (possibly via conducting an isocaloric TRE)

(2) directly comparing effects of eTRE(early TRE) and lTRE(late TRE)

(3) Comparing varying eating window duration

(4) in long-term studies

(5) in a large number of study participants

feasibility of TRE interventions (e.g., timing and duration of eating windows)

+ long-term adherence

+ metabolic benefits

Intermittent Fasting and Obesity-Related Health Outcomes
An Umbrella Review of Meta-analyses of Randomized Clinical Trials

JAMA Network Open. 2021;4(12):e2139558.

Intermittent Fasting and Obesity-Related Health Outcomes
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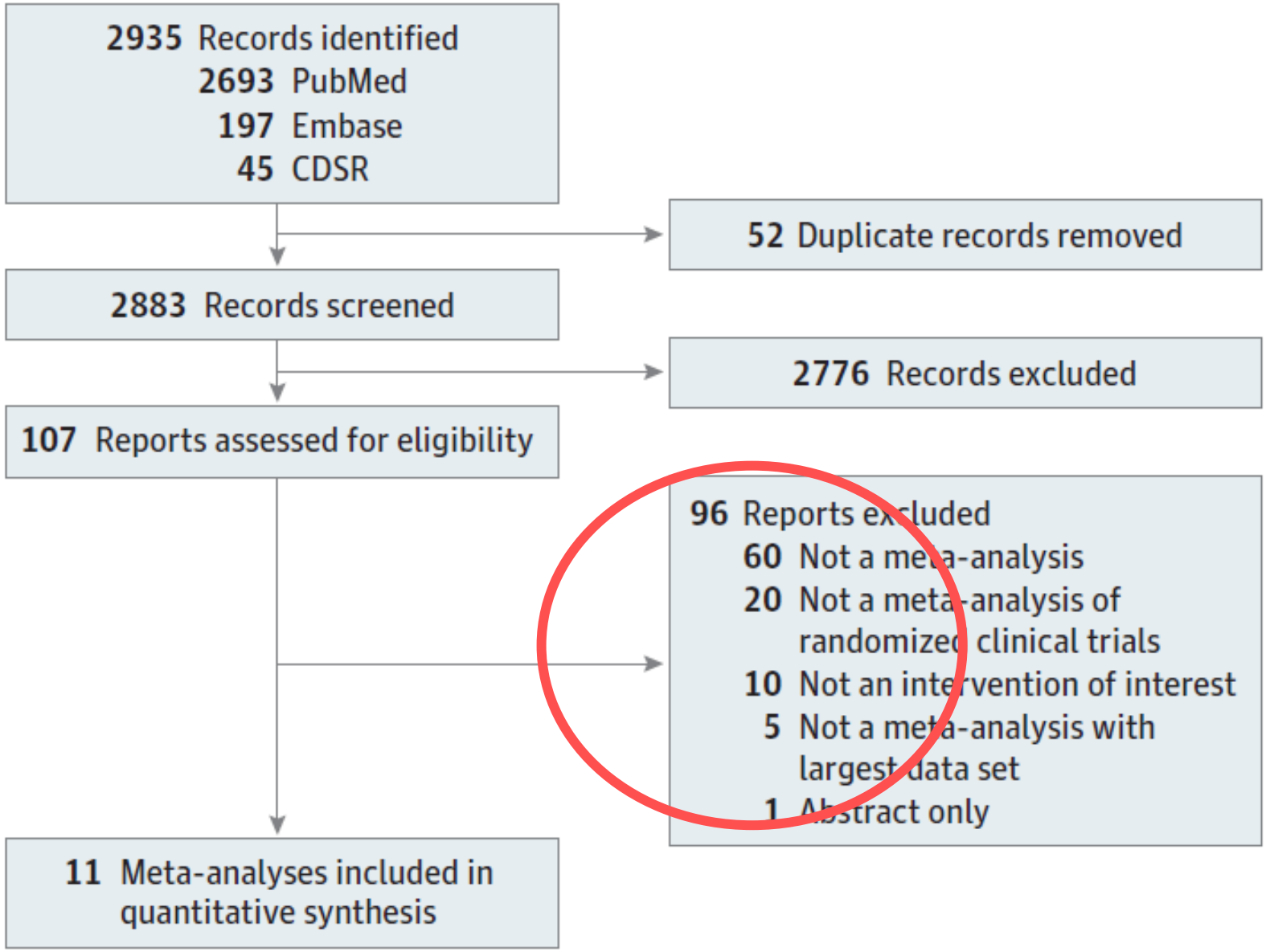

Not a meta-analysis of randomized controlled trials (n = 20)	1. Kul S, Savaş E, Öztürk ZA, Karadağ G. Does Ramadan fasting alter body weight and blood lipids and fasting blood glucose in a healthy population? A meta-analysis. *J Relig Health*. Jun 2014;53(3):929-42. doi:10.1007/s10943-013-9687-0 2. Sadeghirad B, Motaghipisheh S, Kolahdooz F, Zahedi MJ, Haghdoost AA. Islamic fasting and weight loss: a systematic review and meta-analysis. *Public Health Nutr*. Feb 2014;17(2):396-406. doi:10.1017/s1368980012005046 3. Bragazzi NL. Ramadan fasting and chronic kidney disease: Does estimated glomerular filtration rate change after and before Ramadan? Insights from a mini meta-analysis. Article. *International Journal of Nephrology and Renovascular Disease*. 2015;8:53-57. doi:10.2147/IJNRD.S61718 4. Turin TC, Ahmed S, Shommu NS, et al. Ramadan fasting is not usually associated with the risk of cardiovascular events: A systematic review and meta-analysis. J Family Community Med. May-Aug 2016;23(2):73-81. doi:10.4103/2230-8229.181006 5. Glazier JD, Hayes DJL, Hussain S, et al. The effect of Ramadan fasting during pregnancy on perinatal outcomes: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. Oct 25 2018;18(1):421. doi:10.1186/s12884-018-2048-y
	6. Aydin N, Kul S, Karadağ G, Tabur S, Araz M. Effect of Ramadan fasting on glycaemic parameters & body mass index in type II diabetic patients: A meta-analysis. *Indian J Med Res*. Dec 2019;150(6):546-556. doi:10.4103/ijmr.IJMR_1380_17 7. Binsalih S, Al Sayyari RA, Sheikho M, Hejaili FF, Al Sayyari AA. Effect of Fasting the Whole Month of Ramadan on Renal Function Among Muslim Patients With Kidney Transplant: A Meta-Analysis. *Exp Clin Transplant*. Oct 2019;17(5):588-593. doi:10.6002/ect.2019.0245 8. Faris MAIE, Jahrami HA, Obaideen AA, Madkour MI. Impact of diurnal intermittent fasting during Ramadan on inflammatory and oxidative stress markers in healthy people: Systematic review and meta-analysis. Review. *Journal of Nutrition and Intermediary*

	9. Fernando HA, Zibellini J, Harris RA, Seimon RV, Sainsbury A. Effect of Ramadan Fasting on Weight and Body Composition in Healthy Non-Athlete Adults: A Systematic Review and Meta-Analysis. Nutrients. Feb 24 2019;11(2)doi:10.3390/nu11020478 10. Mirmiran P, Bahadoran Z, Gaeini Z, Moslehi N, Azizi F. Effects of Ramadan intermittent fasting on lipid and lipoprotein parameters: An updated meta-analysis. *Nutr Metab Cardiovasc Dis*. Sep 2019;29(9):906-915. doi:10.1016/j.numecd.2019.05.056
Not a meta-analysis with the largest data set (n = 5)	1. Alhamdan BA, Garcia-Alvarez A, Alzahrnai AH, et al. Alternate-day versus daily energy restriction diets: which is more effective for weight loss? A systematic review and meta-analysis. Review. Obesity Science and Practice. 2016;2(3):293-302. doi:10.1002/osp4.52 2. Headland M, Clifton PM, Carter S, Keogh JB. Weight-Loss Outcomes: A Systematic Review and Meta-Analysis of Intermittent Energy Restriction Trials Lasting a Minimum of 6 Months. *Nutrients*. Jun 8 2016;8(6)doi:10.3390/nu8060354 3. Harris L, McGarty A, Hutchison L, Ells L, Hankey C. Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis. *Obes Rev*. Jan 2018;19(1):1-13. doi:10.1111/obr.12593 4. Yan S, Wang C, Zhao H, et al. Effects of fasting intervention regulating anthropometric and metabolic parameters in subjects with overweight or obesity: a systematic review and meta-analysis. *Food Funct*. May 1 2020;11(5):3781-3799. doi:10.1039/d0fo00287a 5. Wang X, Yan Q, Liao Q, et al. Effects of intermittent fasting diets on plasma concentrations of inflammatory biomarkers: A systematic review and meta-analysis of randomized controlled trials. Review. *Nutrition*. 2020;79-80doi:10.1016/j.nut.2020.110974

Meta-analyses of Randomized Clinical Trials Studying Intermittent Fasting

Source	Population	Type of IF	Comparator	Duration of fasting	No. of included studies	Total participants	Outcomes	AMSTAR-2 rating
Cioffi et al,[22] 2018	Adults with or without medical conditions	5:2 diets, MADF	CER	2-6 mo	11	630	Body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, HbA_{1c}, fasting insulin, HOMA-IR, adverse events	Moderate
Harris et al,[23] 2018	Adults with overweight or obesity	5:2 diets, MADF	RD or CER	3-6 mo	6	360	Body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TG, TC, FPG, insulin, SBP, DBP, adverse events	Moderate
Cho et al,[6] 2019	Adults without diabetes	MADF, TRE, 0-calorie ADF	RD or CER	1-6 mo	12	545	BMI, body weight, fat-free mass, fat mass, FPG, HOMA-IR, adiponectin, leptin	Low
Roman et al,[24] 2019	Adults with overweight or obesity	5:2 diets, MADF	CER	1-12 mo	9	782	Body weight, fat-free mass, fat mass, hip circumference, waist circumference	Low
Cui et al,[25] 2020	Adults	MADF	RD	1-12 mo	7	269	BMI, body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, HOMA-IR, SBP, DBP	Low
Meng et al,[7] 2020	Adults	5:2 diets, MADF	RD or CER	1-12 mo	28	1528	HDL-C, LDL-C, TC, TG	Moderate
Moon et al,[5] 2020	Adults	TRE	RD or CER	4 d to 3 mo	19	475	Body weight, fat-free mass, fat mass, HDL-C, LDL-C, TG, FPG, SBP, DBP	Moderate
Park et al,[28] 2020	Adults	MADF	RD, CER, or TRE	1-8 mo	8	728	BMI, body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TC, TG, FPG, insulin, SBP, DBP, CRP	Moderate
Pellegrini et al,[26] 2020	Adults who are healthy or with chronic disease not impacting outcomes	TRE	RD or CER	1-2 mo	11	452	BMI, body weight, fat-free mass, fat mass, HDL-C, LDL-C, TC, TG, FPG, fasting insulin, HOMA-IR, SBP, DBP	Low
Pureza et al,[8] 2020	Adults with overweight or obesity	TRE	RD or TRE	1 d to 3 mo	8	264	LDL-C, HDL-C, TC, TG, FPG, fasting insulin, HOMA-IR, ghrelin	Moderate
He et al,[27] 2021	Adults with overweight or obesity	5:2 diets, MADF	CER	3-12 mo	11	850	Body weight, fat-free mass, fat mass, waist circumference, HDL-C, LDL-C, TC,	Moderate

Intermittent Fasting and Obesity-Related Health Outcomes
An Umbrella Review of Meta-analyses of Randomized Clinical Trials

- MADF (2~6mon), the 5:2 diet(3~6mon) : overweight/obesity 에서 calory restriction group or standard diet group 에 비해 연구 초기에는(단기) 유의한 체중감량 결과도 있음.
  6개월 이후 체중감량에서 유의성 사라짐.

- MADF (obesity) – fat-free mass loss (첫 6개월, −0.70 kg; 95%CI, −1.38 to −0.02) 보였으나, 이후 6 ~12 개월에서는 역시 통계적 유의성 사라짐. (−0.01 kg; 95%CI, −0.68 to 0.69).

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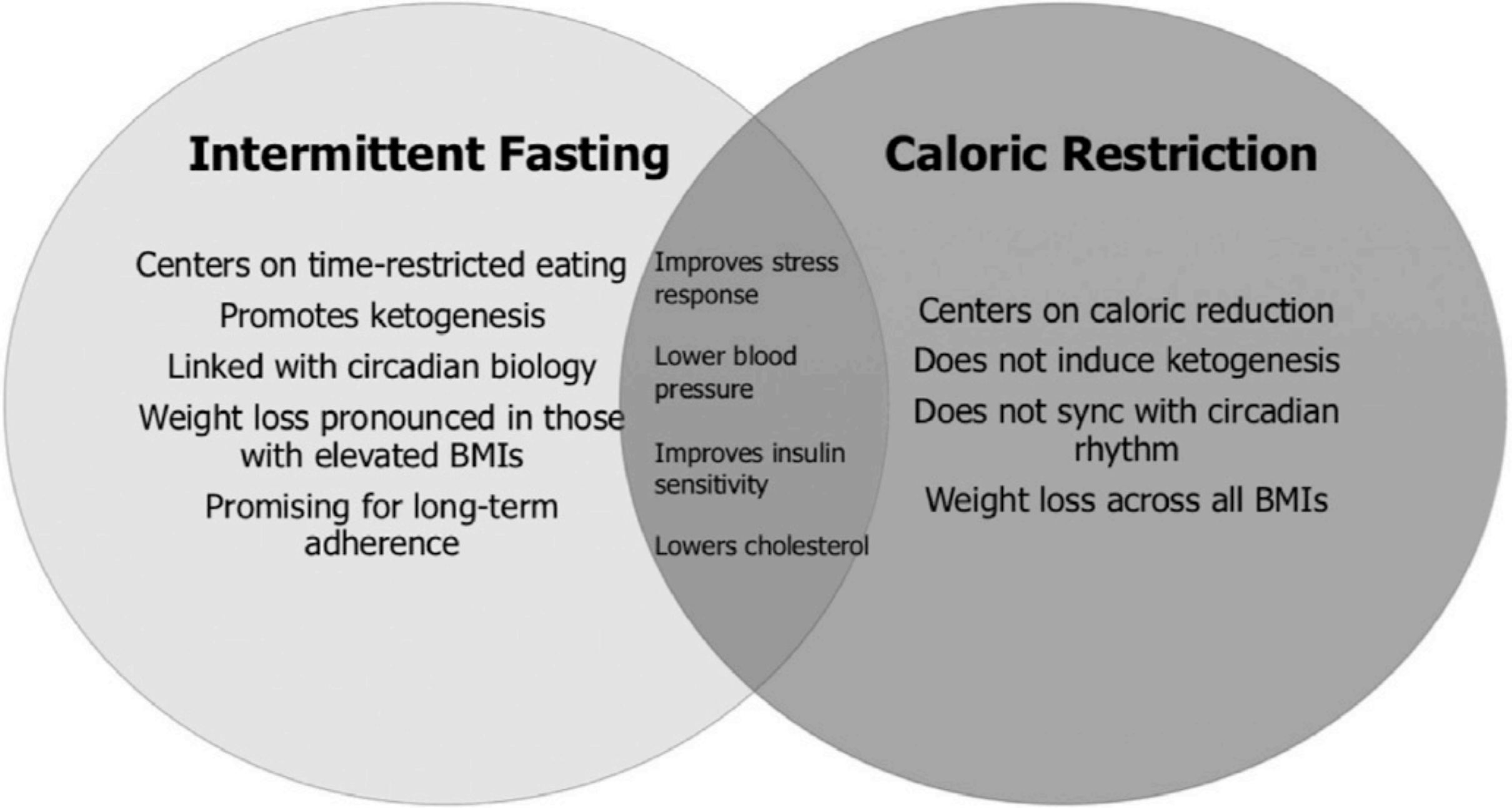
Intermittent Fasting
Centers on time-restricted eating
Promotes ketogenesis
Linked with circadian biology
Weight loss pronounced in those with elevated BMIs
Promising for long-term adherence
Improves stress response
Lower blood pressure
Improves insulin sensitivity
Lowers cholesterol
Caloric Restriction
Centers on caloric reduction
Does not induce ketogenesis
Does not sync with circadian rhythm
Weight loss across all BMIs

Considerations

개인별 선택

- 체중 감소: 간헐적 단식만의 효과? + 총칼로리 감소효과?
- Dropout 비율, 지속가능성
- 식사시간대의 폭식 가능성. 자유롭게 먹지만 폭식은 하지 말자
- 기저질환 및 개인별 차이.

경청해주셔서
감사합니다.