

-
- Fasting is not starvation
 - Good news: Hunger pangs go away!
 - Less work, less shopping, less cleaning, save money



Intermittent Fasting and Metabolic Health

- **. Introduction**

- Obesity and metabolic syndrome (MetS. i.e., insulin resistance, obesity, HTN, and lipids) are a growing problem all across the globe.
- There has been an increasing focus among the medical community to come up with innovative therapies to counter their pathophysiological effects.
- Intermittent fasting is one such tool that has been proposed repeatedly by health experts due to its benefits on the metabolic syndrome.

Izzah Vasim , Chaudry N. Majeed and Mark D. DeBoer, *Nutrients* **2022**, *14*, 631.
<https://doi.org/10.3390/nu14030631> <https://www.mdpi.com/journal/nutrients> *Nutrients*
2022, *14*, 631

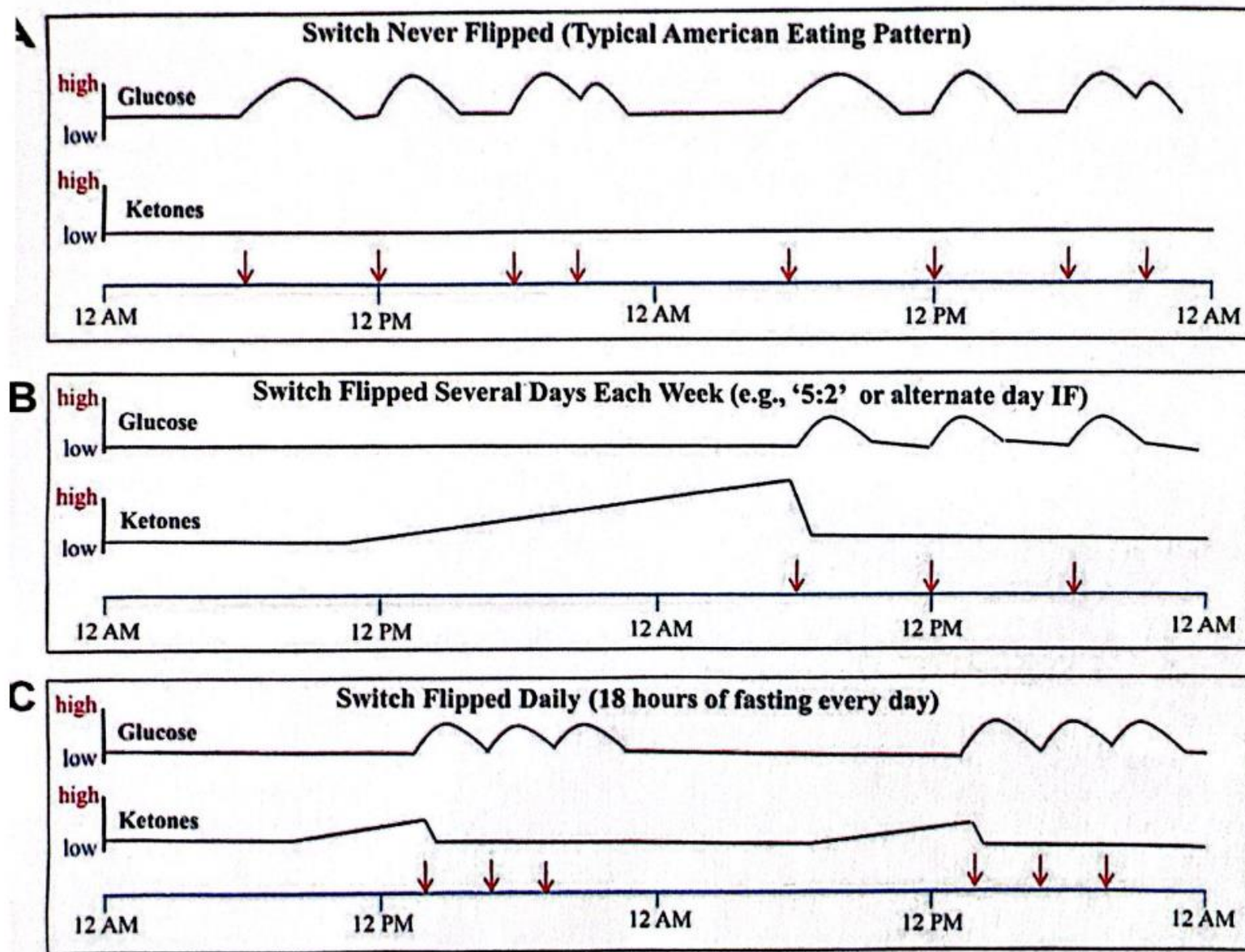
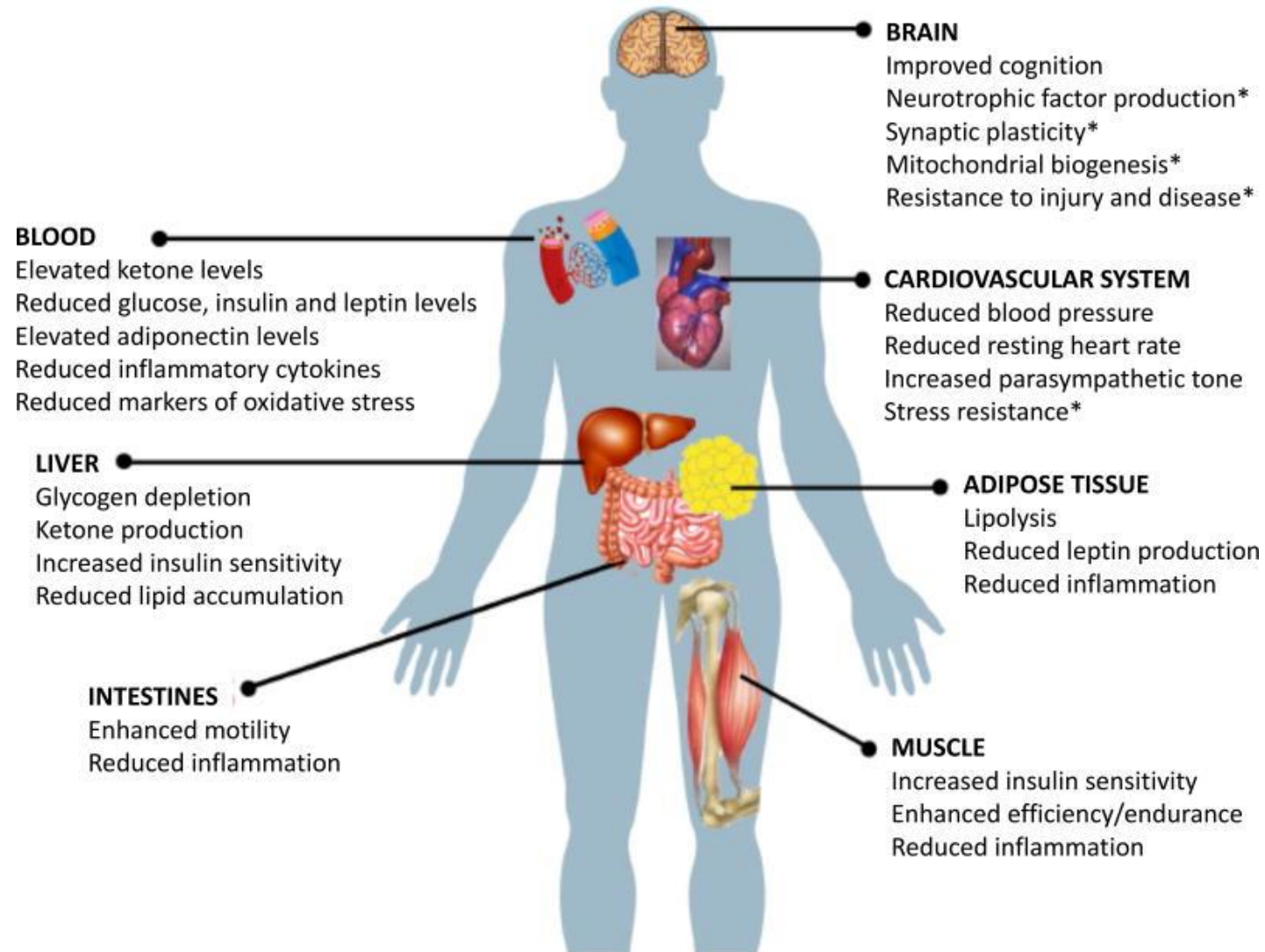


Figure 1. Glucose and ketone levels over the course of three meal eating patterns. (A) The standard meal pattern of three meals daily does not result in an appreciable rise in ketone levels. (B) The 5:2 or alternate-day fasting pattern allows ketones to rise during prolonged fasting, followed by suppressed ketones during the typical feeding day. (C) When meals are compressed to a 6-h period each day, ketones are able to rise during the time between feeding periods. From Anton et al., *Obesity* 2018:

Examples of functional effects and major cellular and molecular responses of various organ systems to IF



d for activities of different intensities and durations.

[10.3 Fuel Sources for Exercise – Introduction to Nutrition and Wellness \(pressbooks.pub\)](#)

| Activity Intensity | Activity Duration | Preferred Fuel | Oxygen Needed? | Activity Example |
|--------------------|-------------------|----------------|----------------|------------------|
| Very high | 30 sec – 3 min | Glucose | No – anaerobic | Sprinting |
| High | 3 min – 20 min | Glucose | Yes aerobic – | Jogging |
| Low to moderate | >20 min | Fat | Yes – aerobic | Walking |

Alternate Day Fasting and Endurance Exercise Combine to Reduce Body Weight and Favorably Alter Plasma Lipids in Obese Humans

- Surabhi Bhutani, Monica C. Klempel, Cynthia M. Kroeger, John F. Trepanowski and Krista A. Varady
- Obesity (2013) 21, 1370-1379. doi:10.1002/oby.20353

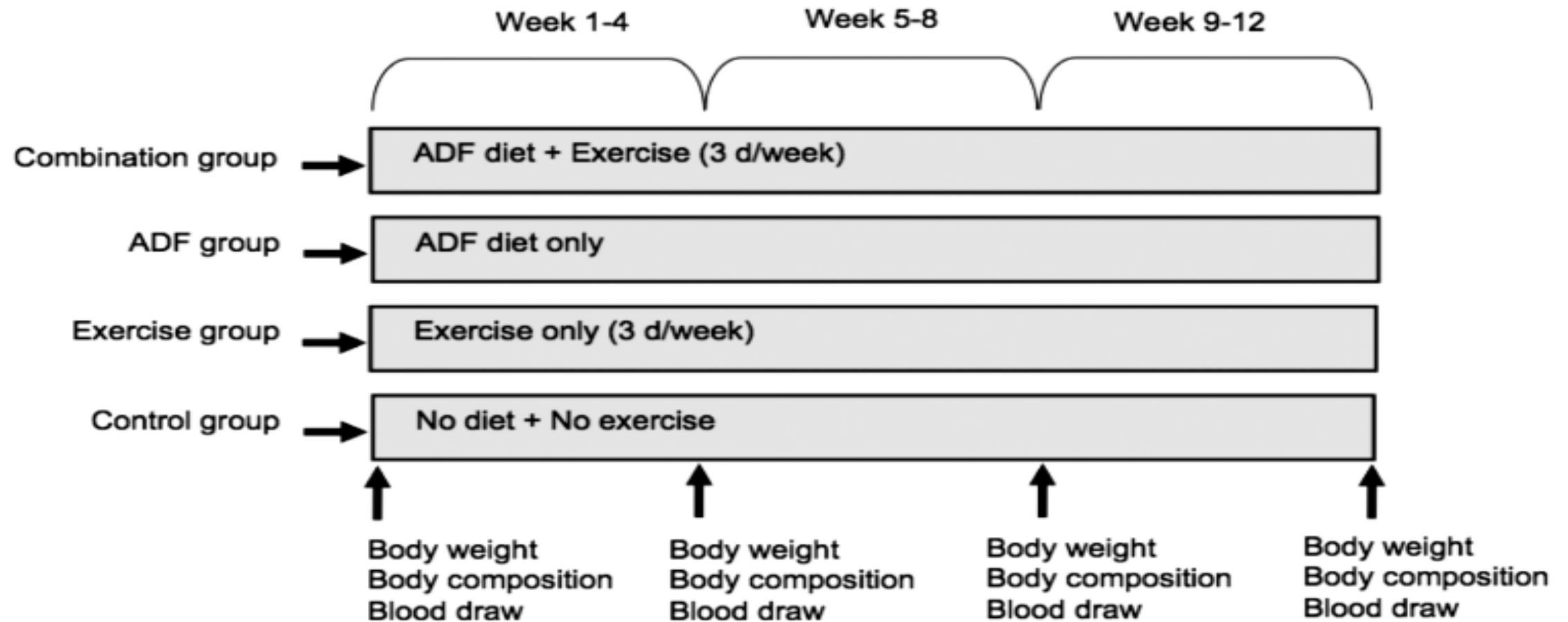


FIGURE 2 Experimental design.

Obesity Alternate Day Fasting and Exercise for Weight Loss Bhutani et al.1372 Obesity | VOLUME 21 | NUMBER 7 | JULY 2013 www.obesityjournal.org

Original Article

CLINICAL TRIALS: BEHAVIOR, PHARMACOTHERAPY, DEVICES, SURGERY

Obesity

TABLE 3 Body weight and body composition during the 12-week trial

| | Intervention | Week 1 | Week 12 | P-value ^a | P-value ^b | Change ^c | P-value ^d |
|--------------------------------------|--------------|---------|---------|----------------------|----------------------|---------------------|----------------------|
| Body weight (kg) | Combination | 91 ± 6 | 85 ± 6 | <0.001 | 0.393 | -6 ± 4 ^a | <0.001 |
| | ADF | 94 ± 3 | 91 ± 3 | <0.001 | | -3 ± 1 ^b | |
| | Exercise | 93 ± 2 | 92 ± 2 | 0.027 | | -1 ± 0 ^b | |
| | Control | 93 ± 5 | 93 ± 5 | 0.577 | | 0 ± 0 ^c | |
| Body mass index (kg/m ²) | Combination | 35 ± 1 | 33 ± 1 | <0.001 | 0.334 | -2 ± 0 ^a | <0.001 |
| | ADF | 35 ± 1 | 34 ± 1 | <0.001 | | -1 ± 0 ^b | |
| | Exercise | 35 ± 1 | 34 ± 1 | 0.030 | | -1 ± 0 ^b | |
| | Control | 35 ± 1 | 35 ± 1 | 0.707 | | 0 ± 0 ^c | |
| Fat mass (kg) | Combination | 45 ± 2 | 40 ± 2 | <0.001 | 0.054 | -5 ± 1 ^a | <0.001 |
| | ADF | 43 ± 2 | 41 ± 2 | 0.008 | | -2 ± 1 ^b | |
| | Exercise | 46 ± 2 | 45 ± 2 | 0.182 | | -1 ± 0 ^b | |
| | Control | 43 ± 4 | 43 ± 4 | 0.570 | | 0 ± 1 ^b | |
| Fat free mass (kg) | Combination | 46 ± 2 | 46 ± 2 | 0.221 | 0.299 | 0 ± 1 | 0.527 |
| | ADF | 51 ± 2 | 50 ± 2 | 0.031 | | -1 ± 1 | |
| | Exercise | 48 ± 1 | 47 ± 1 | 0.321 | | -1 ± 0 | |
| | Control | 50 ± 2 | 49 ± 2 | 0.693 | | -1 ± 1 | |
| Waist circumference (cm) | Combination | 96 ± 2 | 88 ± 1 | <0.001 | 0.310 | -8 ± 1 ^a | <0.001 |
| | ADF | 100 ± 2 | 95 ± 2 | <0.001 | | -5 ± 1 ^b | |
| | Exercise | 98 ± 2 | 95 ± 2 | <0.001 | | -3 ± 1 ^b | |
| | Control | 98 ± 3 | 97 ± 2 | 0.640 | | -1 ± 1 ^b | |

Value reported as mean ± SEM. Intention to treat analysis. ADF: Alternate day fasting.

^aP-value between week 1 and week 12: Repeated-measures ANOVA.

^bP-value between groups at week 12: One-way ANOVA.

^cAbsolute change between week 1 and week 12 values.

^dP-value between groups for absolute change: One-way ANOVA. Means not sharing a common superscript letter are significantly different (Tukey post-hoc test).

| | | | | | | |
|-----------------------------------|-------------|-----------|-----------------------|-------|-------|----------|
| Systolic BP (mm Hg) ^e | Control | 97 ± 13 | 102 ± 11 | 0.452 | 0.176 | 7 ± 6 |
| | Combination | 113 ± 3 | 111 ± 3 | 0.262 | | 5 ± 7 |
| | ADF | 124 ± 3 | 120 ± 3 | 0.007 | | -2 ± 2 |
| | Exercise | 113 ± 2 | 115 ± 3 | 0.284 | | -3 ± 1 |
| Diastolic BP (mm Hg) ^e | Control | 122 ± 5 | 120 ± 6 | 0.603 | 0.123 | 2 ± 2 |
| | Combination | 76 ± 2 | 76 ± 2 | 0.939 | | -2 ± 3 |
| | ADF | 82 ± 2 | 80 ± 2 | 0.034 | | 0 ± 3 |
| | Exercise | 76 ± 2 | 76 ± 2 | 0.976 | | -2 ± 2 |
| Heart rate (bpm) | Control | 86 ± 2 | 84 ± 4 | 0.480 | 0.198 | 0 ± 2 |
| | Combination | 78 ± 2 | 76 ± 2 | 0.384 | | -2 ± 3 |
| | ADF | 75 ± 2 | 75 ± 2 | 0.711 | | -2 ± 2 |
| | Exercise | 71 ± 2 | 71 ± 2 | 0.925 | | 0 ± 1 |
| Fasting glucose (mg/dl) | Control | 76 ± 3 | 77 ± 3 | 0.763 | 0.021 | 0 ± 2 |
| | Combination | 94 ± 2 | 92 ± 3 ^a | 0.589 | | 1 ± 5 |
| | ADF | 98 ± 5 | 95 ± 5 ^a | 0.146 | | -2 ± 4 |
| | Exercise | 92 ± 2 | 91 ± 2 ^{a,b} | 0.862 | | -3 ± 2 |
| Fasting insulin (μIU/ml) | Control | 109 ± 7 | 111 ± 6 ^b | 0.637 | 0.436 | -1 ± 2 |
| | Combination | 14 ± 2 | 11 ± 2 | 0.305 | | 2 ± 4 |
| | ADF | 23 ± 8 | 21 ± 8 | 0.050 | | -21 ± 15 |
| | Exercise | 11 ± 1 | 11 ± 1 | 0.666 | | -7 ± 6 |
| HOMA-IR | Control | 25 ± 4 | 21 ± 4 | 0.178 | 0.396 | 0 ± 8 |
| | Combination | 3 ± 1 | 3 ± 0 | 0.296 | | -16 ± 9 |
| | ADF | 7 ± 3 | 7 ± 3 | 0.092 | | 0 ± 17 |
| | Exercise | 3 ± 0 | 3 ± 0 | 0.782 | | 0 ± 7 |
| C-reactive protein (mg/dl) | Control | 7 ± 2 | 7 ± 2 | 0.165 | 0.943 | 0 ± 10 |
| | Combination | 0.5 ± 0.2 | 0.5 ± 0.2 | 0.488 | | 0 ± 11 |
| | ADF | 0.5 ± 0.1 | 0.5 ± 0.1 | 0.344 | | 0 ± 28 |
| | Exercise | 0.5 ± 0.1 | 0.5 ± 0.1 | 0.200 | | 0 ± 12 |

TABLE 5 LDL particle size during the 12-week trial

| | Intervention | Week 1 | Week 12 | P-value ^a | P-value ^b | Change ^c | P-value ^d |
|--------------------------|--------------|---------|----------------------|----------------------|----------------------|----------------------|----------------------|
| LDL particle size (Å) | Combination | 260 ± 1 | 264 ± 2 ^a | <0.001 | 0.031 | 4 ± 1 ^a | 0.010 |
| | ADF | 261 ± 1 | 266 ± 1 ^a | <0.001 | | 5 ± 1 ^a | |
| | Exercise | 261 ± 2 | 262 ± 2 ^b | 0.426 | | 1 ± 1 ^b | |
| | Control | 259 ± 1 | 260 ± 2 ^b | 0.884 | | 0 ± 1 ^b | |
| Large LDL particles (%) | Combination | 38 ± 4 | 45 ± 5 ^a | 0.142 | 0.014 | 7 ± 5 | 0.064 |
| | ADF | 36 ± 3 | 51 ± 4 ^a | <0.001 | | 15 ± 3 | |
| | Exercise | 39 ± 3 | 40 ± 4 ^b | 0.792 | | 1 ± 5 | |
| | Control | 30 ± 3 | 31 ± 4 ^b | 0.883 | | 1 ± 4 | |
| Medium LDL particles (%) | Combination | 37 ± 2 | 38 ± 2 | 0.845 | 0.301 | 1 ± 3 | 0.817 |
| | ADF | 37 ± 1 | 35 ± 1 | 0.288 | | -2 ± 2 | |
| | Exercise | 41 ± 3 | 40 ± 3 | 0.453 | | -1 ± 2 | |
| | Control | 41 ± 2 | 40 ± 2 | 0.717 | | -1 ± 2 | |
| Small LDL particles (%) | Combination | 25 ± 3 | 18 ± 3 ^a | 0.010 | | -7 ± 2 ^a | 0.007 |
| | ADF | 27 ± 3 | 15 ± 3 ^a | <0.001 | 0.023 | -12 ± 3 ^a | |
| | Exercise | 21 ± 3 | 20 ± 4 ^b | 0.972 | | -1 ± 4 ^b | |
| | Control | 29 ± 3 | 30 ± 3 ^b | 0.776 | | 1 ± 3 ^b | |

Value reported as mean ± SEM. Intention to treat analysis. ADF: Alternate day fasting. Large LDL particles (>260 Å), medium LDL particles (255-260 Å), and small LDL particles (<255 Å).

^aP-value between week 1 and week 12: Repeated-measures ANOVA.

^bP-value between groups at week 12: One-way ANOVA. Means not sharing a common superscript letter are significantly different (Tukey post-hoc test).

^cAbsolute change between week 1 and week 12 values.

^dP-value between groups for absolute change: One-way ANOVA. Means not sharing a common superscript letter are significantly different (Tukey post-hoc test).

Rating of Perceived Exertion (RPE) Category Scale

- 6
- 7 Very, very light
- 8
- 9 Very light
- 10
- 11 Fairly light
- 12
- 13 Somewhat hard
- 14
- 15 Hard
- 16
- 17 Very hard
- 18
- 19 Very, very hard
- 20

Borg G. Borg's Perceived Exertion and Pain Scales. Champaign, IL: Human Kinetics, 1998.

Rating of Perceived Exertion (RPE) Category-Ratio Scale

- 0 Nothing at all
- 0.3
- 0.5 Extremely weak Just noticeable
- 0.7
- 1 Very weak
- 1.5
- 2 Weak Light
- 2.5
- 3 Moderate
- 4
- 5 Strong Heavy
- 6
- 7 Very strong
- 8
- 9
- 10 Extremely strong "Maximal"
- 11
- Absolute maximum Highest Possible

Borg G. Borg's Perceived Exertion and Pain Scales. Champaign, IL: Human Kinetics, 1998.

How can we incorporate it safely?

- Should be alright for most patients
- Start cautiously
- Listen to your body
- Caution for Type 2 diabetic taking diabetic medications including insulin, GLP 1 analogues, etc.
- Contraindicated in Type 1 diabetics and pregnant women



Summary of the major metabolic pathways involved in the metabolic switch and responses of excitable cells to the ketone β -hydroxybutyrate (β -OHB). See text for description. AcAc, acetoacetate; ATP, adenosine

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[Obesity \(Silver Spring\)](#). 2018 Feb; 26(2): 254–268.
 Published online 2017 Oct 31. doi: [10.1002/oby.22065](#)
 PMID: PMC5783752
 NIHMSID: NIHMS912771
 PMID: [29086496](#)

Flipping the Metabolic Switch: Understanding and Applying Health Benefits of Fasting

[Stephen D. Anton](#),¹ [Keelin Moehl](#),² [William T. Donahoe](#),³ [Krisztina Marosi](#),² [Stephanie Lee](#),¹ [Arch G. Mainous, III](#),⁴ [Christiaan Leeuwenburgh](#),¹ and [Mark P. Mattson](#)^{2,5}
 iphosphate; FFA, free fatty acids; TCA, tricarboxylic acid.

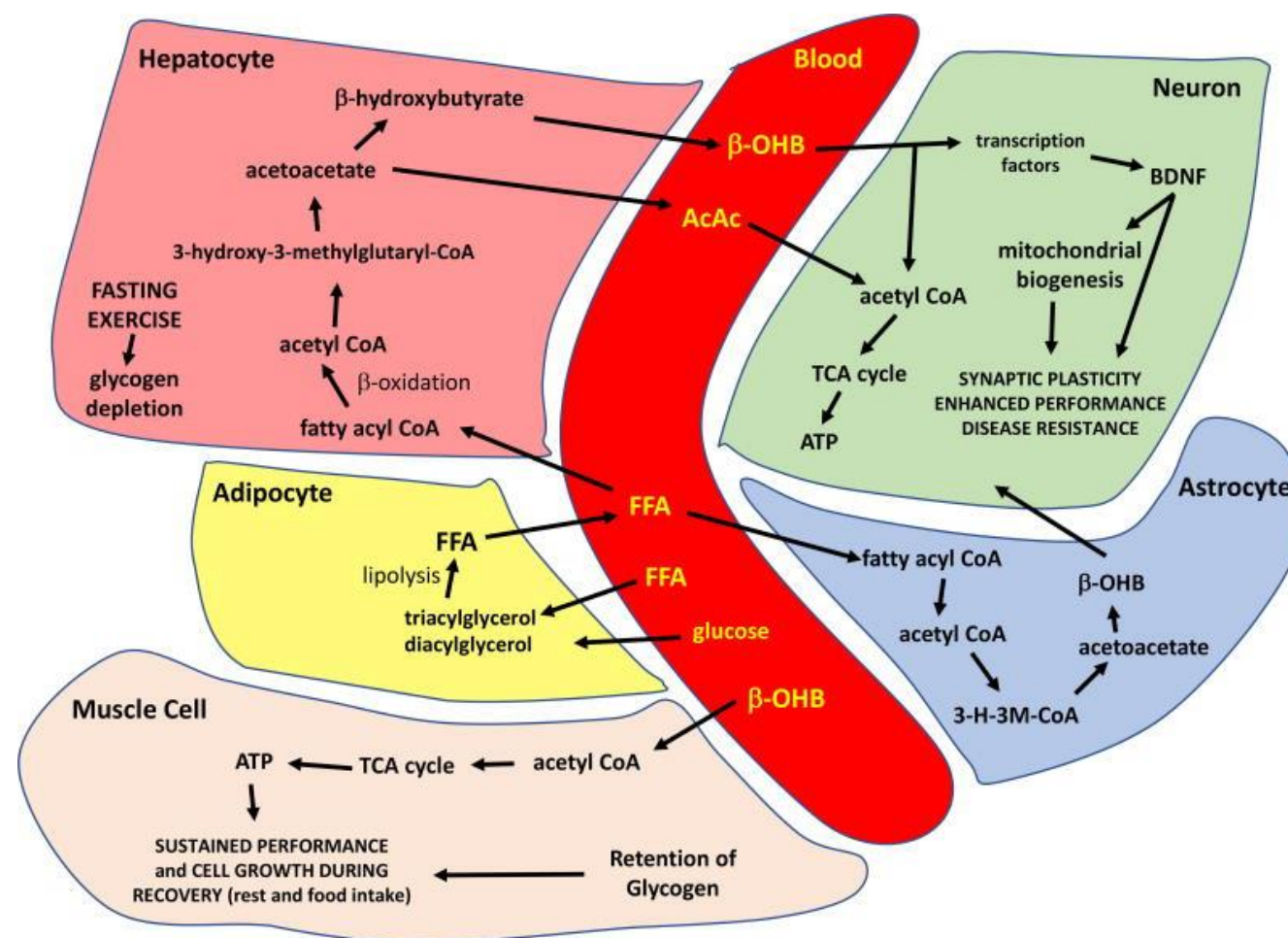


Figure 10.1. Anaerobic vs aerobic metabolism. Note that carbohydrate is the only fuel utilized in anaerobic metabolism, but all three macronutrients can be used for fuel during aerobic metabolism.

