Hypothesis

Biology

# Accelerate Self-Catabolism of Adipose Tissue
## A Promising Way for Weight Loss

**Inés von Yamin***
Universidad de Buenos Aires, Viamonte 430 (and/or 444) and Reconquista 694, Buenos Aires, C1053 CABA, Argentina
*: All correspondence should be sent to: Dr. Inés von Yamin
*Author's Contact*: Dr. Inés von Yamin, Ph.D., E-mail: inesyamin@hotmail.com
*DOI*: https://doi.org/10.15354/si.25.hp022
*Funding*: No funding source declared.
*COI*: The author declares no competing interest.
*AI Declaration*: The author affirms that artificial intelligence did not contribute to the process of preparing the work.

**Obesity is a multifaceted global health concern associated with numerous chronic diseases, including cardiovascular conditions, type 2 diabetes, and certain cancers. Traditional weight loss strategies—such as caloric restriction, exercise, and pharmacotherapy—have yielded inconsistent results for many individuals. A promising alternative lies in the body's own capability to mobilize and catabolize adipose tissue. This hypothesis article explores the concept of accelerating self-catabolism of adipose tissue as a targeted and efficient method for sustainable weight loss. Drawing from advances in metabolic physiology, hormonal signaling, mitochondrial function, and gene expression, the paper posits that enhancing lipolytic pathways, modulating adipokines, and leveraging brown adipose tissue (BAT) thermogenesis could synergistically increase energy expenditure while reducing fat mass. I hypothesized that integrated interventions, including selective pharmacologic agents, thermogenic stimulation, and intermittent fasting, to activate endogenous fat-burning mechanisms. Ultimately, this approach may redefine obesity treatment paradigms by transforming fat tissue from a passive energy store into an active agent of weight loss.**

**Keywords**: Obesity; Weight Loss; Self-Catabolism; Adipose Tissue; Health

Science Insights, July 31, 2025; Vol. 47, No. 1, pp.1889-1892.



OBESITY has reached epidemic proportions globally, posing a severe public health challenge with significant implications for morbidity, mortality, and healthcare expenditures. While the etiology of obesity is complex, encompassing genetic, environmental, and behavioral factors, it is fundamentally a disorder of energy imbalance—where energy intake chronically exceeds expenditure. Existing strategies for weight loss—dietary modification, increased physical activity, behavioral therapy, and pharmacologic treatments—often achieve only modest and transient results (Christoffersen et al., 2022). Surgical interventions like bariatric surgery offer more substantial outcomes but are invasive and not without complications. There remains an unmet need for more effective, sustainable, and accessible solutions. One potentially revolutionary approach involves harnessing and enhancing the body's intrinsic mechanisms of adipose tissue breakdown—termed

self-catabolism of adipose tissue—to accelerate fat loss and improve metabolic health.

Adipose tissue, traditionally viewed as a passive reservoir for energy storage, is now recognized as an active endocrine organ involved in metabolic regulation. It exists in different forms—white adipose tissue (WAT), which stores energy, and brown adipose tissue (BAT), which dissipates energy through thermogenesis (Cao et al., 2021). Beige adipocytes, which are inducible thermogenic cells within WAT depots, further complicate this dichotomy. Mobilizing and increasing the catabolic activity within these adipose tissues holds the key to altering body composition and promoting weight loss from within.

Lipolysis is the fundamental process of triglyceride breakdown in adipocytes into free fatty acids (FFAs) and glycerol. Under normal physiological conditions, this process is tightly regulated by hormonal signals—most notably catecholamines, insulin, glucagon, and natriuretic peptides (Nielsen et al., 2014). Catecholamines, through β-adrenergic receptor activation, stimulate cyclic AMP (cAMP) production, activating protein kinase A (PKA) and phosphorylating hormone-sensitive lipase (HSL) and perilipin, thereby promoting lipolysis (Althaher, 2022). Conversely, insulin suppresses lipolysis by activating phosphodiesterase, which degrades cAMP. A hypothesis that proposes accelerating self-catabolism of adipose tissue must therefore consider ways to upregulate lipolytic signaling while mitigating anti-lipolytic factors.

One promising method is the pharmacological activation of β3-adrenergic receptors, predominantly expressed in adipocytes. Agents like mirabegron, originally developed for overactive bladder, have shown efficacy in activating BAT and inducing thermogenesis in humans (Dehvari et al., 2017). By stimulating BAT and increasing energy expenditure, such agents may drive a net negative energy balance without requiring dietary restriction. Furthermore, stimulating BAT not only burns calories but also enhances glucose metabolism, offering additional benefits for insulin sensitivity and glycemic control. Another approach involves targeting the enzyme AMP-activated protein kinase (AMPK), a cellular energy sensor that promotes fatty acid oxidation and mitochondrial biogenesis (McCarty, 2013). Activation of AMPK, through agents like metformin or AICAR, may potentiate the catabolic flux within adipose tissues, enhancing energy dissipation.

Moreover, the transition of WAT to beige fat—termed "browning"—presents another mechanism for increasing energy expenditure. Browning is induced by cold exposure, certain hormones (like irisin and FGF21), and β3-adrenergic agonists. Beige adipocytes exhibit UCP1 expression, a mitochondrial protein that uncouples oxidative phosphorylation, allowing energy to be released as heat instead of being stored as ATP (Wankhade et al., 2016). This non-shivering thermogenesis could dramatically increase basal metabolic rate and promote fat loss. Enhancing browning via external stimuli (e.g., cold exposure, exercise) or pharmacologically mimicking this process holds potential for long-term adiposity control.

While stimulating lipolysis is critical, an equally important step is the effective oxidation of FFAs generated from adipose catabolism. Otherwise, elevated FFA levels may result in ectopic fat deposition, lipotoxicity, and insulin resistance. Therefore, strategies to enhance mitochondrial oxidative capacity in skeletal muscle and liver are essential. Nutrients like L-carnitine, which facilitates the transport of FFAs into mitochondria, and polyphenols like resveratrol, which activate SIRT1 and PGC-1α (key regulators of mitochondrial biogenesis), may play a role in supporting the oxidative disposal of mobilized lipids (Vishwanath, 2016).

Intermittent fasting (IF), another emerging intervention, has shown promise in promoting self-catabolism of adipose tissue through metabolic switching. During fasting periods, insulin levels drop, while glucagon and catecholamines rise, favoring lipolysis and ketogenesis. Studies in both animals and humans have shown that IF enhances mitochondrial function, reduces inflammation, and improves insulin sensitivity, in part through increased utilization of fat as fuel (Brocchi et al., 2022; Zhang et al., 2024). This temporal regulation of eating patterns not only creates a caloric deficit but also aligns with the body's natural metabolic rhythms, making it a potentially powerful tool for mobilizing stored fat.

Gene expression patterns in adipose tissue also provide insight into self-catabolic potential. Transcription factors such as PPARγ, PGC-1α, and C/EBPα orchestrate adipogenesis and metabolic activity. Modifying the expression of these genes through diet, drugs, or epigenetic modulation can shift adipose tissue toward a more metabolically active phenotype. For instance, thiazolidinediones, though controversial due to side effects, are known PPARγ agonists that improve insulin sensitivity and modulate adipose function (Akoum, 2014). Nutrigenomic approaches, such as supplementation with omega-3 fatty acids, can also influence gene expression to favor fat oxidation over storage.

Hormonal regulation is another axis through which self-catabolism may be controlled. Leptin, secreted by adipocytes in proportion to fat mass, plays a pivotal role in energy homeostasis by suppressing appetite and promoting energy expenditure (Engineer & Garcia, 2012). However, leptin resistance is common in obesity, blunting these effects. Restoring leptin sensitivity through lifestyle interventions or pharmacologic sensitizers could reinstate its catabolic role. Additionally, adiponectin, an anti-inflammatory adipokine, enhances insulin sensitivity and promotes fatty acid oxidation (Andreoli et al., 2019). Its levels are inversely correlated with fat mass. Enhancing adiponectin secretion or mimicking its activity could serve as another node for promoting fat catabolism.

Environmental and behavioral factors also influence adipose tissue dynamics. Chronic stress, sleep deprivation, and circadian rhythm disruption are known to elevate cortisol levels, which promote visceral fat accumulation and impair insulin sensitivity. Therefore, stress reduction techniques, improved sleep hygiene, and alignment with natural circadian rhythms are integral to maximizing self-catabolism (McEwen, 2008). Exercise, particularly high-intensity interval training (HIIT), not only burns calories but also improves mitochondrial density and insulin sensitivity, augmenting the capacity to oxidize liberated FFAs (Martínez‐Montoro et al., 2023).

Emerging technologies, including wearable thermogenic devices, localized ultrasound stimulation, and low-level laser therapy, are being investigated for their ability to stimulate lo-

calized fat loss by enhancing cellular metabolism. Although still in early stages, these tools offer future promise in activating self-catabolic mechanisms without pharmacologic side effects.

While the above strategies are promising, safety considerations are paramount. Overactivation of lipolysis without sufficient oxidation may lead to elevated circulating FFAs and subsequent hepatic steatosis or cardiac lipid accumulation (Zagkou et al., 2022). Furthermore, prolonged fasting or over-reliance on thermogenic drugs may risk muscle catabolism, nutrient deficiencies, or cardiovascular strain. A comprehensive approach must therefore balance efficacy with safety, perhaps through combination therapies tailored to individual metabolic profiles.

To translate this idea into clinical practice, future research must identify biomarkers predictive of lipolytic responsiveness, develop non-invasive tools for adipose tissue imaging, and conduct longitudinal trials evaluating the long-term efficacy and safety of self-catabolism-promoting interventions. Precision medicine approaches, integrating genomics, metabolomics, and microbiome profiling, could allow for personalized activation of adipose catabolism based on individual biology.

Overall, accelerating the self-catabolism of adipose tissue represents a compelling and biologically plausible strategy for sustainable weight loss. By mobilizing the body's own fat-burning machinery through targeted stimulation of lipolysis, browning, mitochondrial oxidation, and hormonal modulation, this approach seeks to transform adipose tissue from a static energy depot into a dynamic, self-regulating energy consumer. As scientific understanding of adipose tissue complexity evolves, this hypothesis may catalyze the development of next-generation obesity therapies that are not only effective but also physiologically harmonious. Integrating lifestyle, pharmacology, and technology to activate these endogenous pathways could herald a new era in the management of metabolic disorders and obesity-related diseases.■

Received: March 29 , 2025 | Revised: May 04, 2025 | Accepted: May 19, 2025

## References


Akoum, S. E. (2014). PPAR Gamma at the crossroads of health and disease: A MasterChef in metabolic homeostasis. Endocrinology & Metabolic Syndrome, 3(1). DOI: https://doi.org/10.4172/2161-1017.1000126

Althaher, A. R. (2022). An Overview of Hormone-Sensitive Lipase (HSL). The Scientific World JOURNAL, 2022, 1–9. DOI: https://doi.org/10.1155/2022/1964684

Andreoli, M. F., Donato, J., Cakir, I., & Perello, M. (2019). Leptin resensitisation: a reversion of leptin-resistant states. Journal of Endocrinology, 241(3), R81–R96. DOI: https://doi.org/10.1530/joe-18-0606

Brocchi, A., Rebelos, E., Dardano, A., Mantuano, M., & Daniele, G. (2022). Effects of intermittent fasting on brain metabolism. Nutrients, 14(6), 1275. DOI: https://doi.org/10.3390/nu14061275

Cao, Q., Wang, S., Wang, H., Cui, X., Jing, J., Yu, L., Shi, H., & Xue, B. (2021). Fatty acids rescue the thermogenic function of sympathetically denervated brown fat. Biomolecules, 11(10), 1428. DOI: https://doi.org/10.3390/biom11101428

Christoffersen, B. Ø., Sanchez‐Delgado, G., John, L. M., Ryan, D. H., Raun, K., & Ravussin, E. (2022). Beyond appetite regulation: Targeting energy expenditure, fat oxidation, and lean mass preservation for sustainable weight loss. Obesity, 30(4), 841-857. DOI: https://doi.org/10.1002/oby.23374

Dehvari, N., Da Silva, E. D., Junior, Bengtsson, T., & Hutchinson, D. S. (2017). Mirabegron: potential off target effects and uses beyond the bladder. British Journal of Pharmacology, 175(21), 4072–4082. DOI: https://doi.org/10.1111/bph.14121

Engineer, D. R., & Garcia, J. M. (2012). Leptin in anorexia and cachexia syndrome. International Journal of Peptides, 2012, 1–13. DOI: https://doi.org/10.1155/2012/287457

Martínez‐Montoro, J. I., Benítez‐Porres, J., Tinahones, F. J., Ortega‐Gómez, A., & Murri, M. (2023). Effects of exercise timing on metabolic health. Obesity Reviews, 24(10). DOI: https://doi.org/10.1111/obr.13599

McCarty, M. F. (2013). AMPK activation—protean potential for boosting healthspan. AGE, 36(2), 641–663. DOI: https://doi.org/10.1007/s11357-013-9595-y

McEwen, B. S. (2008). Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. European Journal of Pharmacology, 583(2–3), 174–185. DOI: https://doi.org/10.1016/j.ejphar.2007.11.071

Nielsen, T. S., Jessen, N., Jørgensen, J. O. L., Møller, N., & Lund, S. (2014). Dissecting adipose tissue lipolysis: molecular regulation and implications for metabolic disease. Journal of Molecular Endocrinology, 52(3), R199–R222. DOI: https://doi.org/10.1530/jme-13-0277

Vishwanath, V. A. (2016). Fatty Acid Beta-Oxidation Disorders: A Brief Review. Annals of Neurosciences, 23(1), 51–55. DOI: https://doi.org/10.1159/000443556

Wankhade, U. D., Shen, M., Yadav, H., & Thakali, K. M. (2016). Novel browning agents, mechanisms, and therapeutic potentials of brown adipose tissue. BioMed Research International, 2016, 1–15. DOI: https://doi.org/10.1155/2016/2365609

Zagkou, S., Marais, V., Zeghoudi, N., Guillou, E. L., Eskelinen, E., Panasyuk, G., Verrier, B., & Primard, C. (2022). Design and evaluation of Autophagy-Inducing particles for the treatment of abnormal lipid accumulation. Pharmaceutics, 14(7), 1379. DOI: https://doi.org/10.3390/pharmaceutics14071379

Zhang, A., Wang, J., Zhao, Y., He, Y., & Sun, N. (2024). Intermittent fasting, fatty acid metabolism reprogramming, and neuroimmuno microenvironment: mechanisms and application prospects. Frontiers in Nutrition, 11. DOI: https://doi.org/10.3389/fnut.2024.1485632