

## A Review on the Effects of Physical Activity on Ghrelin, an Appetite-Stimulating Hormone

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# Abstract

Ghrelin is a peptide hormone produced by the stomach, which is mainly responsible for appetite regulation. The aim of this review paper is to provide a summary of the current findings on the relationship between the different intensities and modalities of physical activity and ghrelin, and how ghrelin interacts with the brain to stimulate appetite. After reviewing primary and secondary research papers about the relationships between physical exercise and ghrelin, it was found that high-intensity exercise was more likely to increase ghrelin levels than low-intensity exercise, activating hunger signals and stimulating food intake. However, there were inconsistencies in whether different types of exercise (anaerobic and aerobic) increase or decrease ghrelin levels. Although physical activity clearly has effects on ghrelin production, further research is needed to address the clear relationship between the two.

#### Introduction

According to the World Health Organization (WHO), healthy life expectancy is defined as an average number of years that a person can live in "full health", without disease or injury. People are becoming more mindful of living a healthy life nowadays, prioritizing physiological and psychological health. As wellness is a main interest for health-conscious individuals, there is an emerging attention to weight loss trends, healthy diet and exercising. In response to the healthy lifestyle trends, this paper will mainly explore the relationship between different types and intensities of exercise on appetite, a desire for food. Sometimes we feel hungrier after working out, or sometimes we do not even have the energy to eat after an intense workout. As making healthy food choices and being physically active are key steps for a healthy life, the purpose of this paper is to investigate how exercise affects the ghrelin hormone, and how the ghrelin interacts with the brain to stimulate appetite and food-seeking behavior. Ghrelin is a peptide hormone primarily responsible for appetite stimulation. Physical activity type and volume may dictate the change in ghrelin concentration for each individual, which may be influenced by weight loss history (Laura et al., 2010). Food intake, instigated by increased ghrelin concentration, leads to increases in dopamine as well. This activates positive reward pathways in the brain, reinforcing healthy lifestyle actions that maintain homeostasis, a self-regulating process by which an organism tends to maintain stability while adjusting to changing external conditions (Britanicca, 2023). Through exploration of this research topic, individuals will gain a better understanding of the biological pathways that drive food intake and factors influencing this process, proving helpful to health -conscious individuals who wish to learn more about the relationship between their exercise, appetite, and diet.



## Ghrelin

Ghrelin is a peptide hormone consisting of 28 amino acids, which is produced by the stomach. It was discovered as an endogenous ligand for the growth hormone secretagogue receptor (GHS-R), a component of the ghrelin signaling pathway, which signals ghrelin release. There are two isoforms, or functionally similar proteins with different amino acid sequences identified, GHS-R1a and GHS-R1b (Laviano et al., 2012). While GHS-R1b is an inactive variant without a specific function, GHS-R1a is responsible for growth hormone(GH) secretion and stimulation of appetite by acting on the hypothalamic arcuate nucleus, a region in the brain known to control food intake (Nejmeddine et al., 2021).

The two peptide variants of ghrelin are acyl ghrelin (AG) and des-acyl ghrelin (DAG) (Nejmeddine et al., 2021). The ratio of AG and DAG circulating in the bloodstream is dependent on the physiological factors such as body composition and nutritional status, but typically ranges from 1:4 to 1:9. The ratio is normally 1:9 in circulating ghrelin (Ouerghi et al., 2021). AG exerts the hormonal and metabolic actions of ghrelin by binding to GHS-R1a, a receptor that is widely distributed in the brain (Li et al., 2021). On the other hand, DAG is unable to bind to and activate GHSR. Instead, it is responsible for numerous metabolic effects like insulin sensitivity and metabolism, which may antagonize AG effects (Ouerghi et al., 2021). Insulin is a hormone that regulates glucose level in the bloodstream (Rahman et al., 2021). Ghrelin and insulin levels have a reciprocal relationship, where ghrelin suppresses insulin secretion (Muller et al., 2015). Therefore, ghrelin not only influences one's level of desire to eat but also the individual's ability to physiologically process their food intake. This means that ghrelin's function is far more complex than one may initially think.

Ghrelin levels are influenced by a variety of factors, such as habitual eating patterns, body composition, metabolism, and physical activity. For instance, circulating ghrelin levels change depending on meal times and available energetic fuel (Frecka & Mattes., 2008). This suggests that as ghrelin is highly responsive to both internal and external stimuli, we should consider a wide range of factors when investigating the effect of exercise on ghrelin. These may include the type of exercise, timing, and intensity of exercise, an individual's diet, particularly the foods they eat before, during, or after engaging in exercise, and the physical environment. Therefore, depending on actions we take and food we eat, the chemical concentration of ghrelin changes, leading to physical and psychological changes influencing our everyday life.

#### **Ghrelin and Appetite Stimulation**

Ghrelin has diverse physiological functions including the stimulation of the release of growth hormone, regulation of energy metabolism, sleep/wake rhythm, a daily sleeping pattern, and reward seeking behavior such as approach, consumption, and addiction (Carrión & Poppel, 2007). Ghrelin's interaction with the brain plays an important role in appetite stimulation. In a review on ghrelin by Muller and colleagues (2015), researchers state that ghrelin increases food consumption by activating distinct reward centers in the brain. This suggests that food consumption is more than just a physiological mechanism, but is also influenced by psychological factors. Ghrelin acts on hypothalamic and extra-hypothalamic areas of the brain, increasing food motivation along with hunger and satiation signals (Omar et al., 2019). The hypothalamus is an area of the brain that produces hormones that control a wide range of physiological processes needed for homeostasis, including body temperature, heart rate, and



hunger (Johnson, 2023). By linking the nervous system and the endocrine system, this mediates motivational processes (Sternson, 2015). The ventral tegmental area (VTA) is another area of the brain interacting with ghrelin. As the ventral tegmental area contains ghrelin receptors, ghrelin binds to this area and produces a food intake response. It regulates motivational and cognitive functions to gain access to food and to select food that are most rewarding (Rad et al., 2020). Rewarding aspects are crucial in food consumption since food intake is not just a life-supporting process, but a function that influences one's psychological state.

Moreover, ghrelin's interactions with the VTA also influence the processes that occur in this brain area, including the mesolimbic dopamine pathway. Dopamine is a neurotransmitter that is involved in the rewarding aspects of food and the mesolimbic pathway is a key component of food motivational aspects (Omar et al., 2019). As ghrelin directly targets the ventral tegmental area and activates the mesolimbic dopamine pathway, it serves as a key regulator of appetite. Through mediating dopamine release, the VTA plays a key role in the regulation of reward consumption (Cai & Tong, 2022). This may positively reinforce food consumption both when it is physiologically necessary and when this provides psychological satisfaction.

#### **Ghrelin and Physical Activity**

Exercise plays a critical role in regulating energy balance, causing change in fat percentage and body mass. As ghrelin levels are highly dependent on body composition, there is a possible link between exercise and ghrelin levels. It is also important to consider the type, duration, and intensity when discussing the impact of exercise on ghrelin levels. Acute exercise, or a single session of exercise, does not alter ghrelin levels while long-term chronic exercise increases ghrelin levels, which is most likely due to weight loss (Schmidt et al., 2004). Exercise does not influence circulating ghrelin levels independent of weight loss. In terms of intensity, low-intensity exercise stimulates ghrelin while high-intensity exercise is likely to suppress ghrelin. This is most likely due to an increased sympathetic nervous system activity and redistribution of blood flow (Serife et al., 2011). During and after exercise, the sympathetic nervous system speeds up the heart rate and delivers more blood to the body due to the increase in requirements for oxygen in skeletal muscle (Burton et al, 2004).

As mentioned earlier, there are two variants of ghrelin, AG and DAG. DAG is considered unimportant since acylation of ghrelin is essential for appetite regulation. Thus, it is important to consider AG levels instead of total ghrelin (TG) levels when discussing the effect of exercise on ghrelin. AG responds differently to different durations of exercise, acute and chronic. Acute exercise refers to a single-session exercise, whereas chronic exercise is performed over an extended period of time. According to studies, although not always consistent, there is a general trend of increase in AG in response to long-term chronic exercise (Ouerghi et al., 2021). This is because prolonged exercise is likely to produce weight loss. As ghrelin responses are primarily determined by body weight change, exercise does not influence circulating ghrelin levels independent of weight loss (Schmidt et al., 2004). This also explains why increase in AG is more likely to occur among obese individuals than normal weight individuals (Nejmeddine et al., 2021).

However, for the effect of acute exercise, the findings are not consistent. In a study by Hackney and Constantini, it was concluded that different responses were observed in ghrelin levels according to acute exercise. Although there was mostly no change or suppression in AG



concentration after acute exercise, some studies reported that they observed a significant post exercise increase in AG concentration (Broom et al., 2007). This means that the effect of acute exercise on ghrelin cannot be generalized, and we should consider various factors such as body composition and physical activity levels in different individuals. For instance, compared to normal people, athletes who regularly engage in intense physical activity would have high muscle mass and positive energy balance, which would lead to better physical performance, causing a difference in ghrelin concentration. Taking this into account, more studies using subjects with diverse physical backgrounds must be conducted in order to reach a reliable conclusion.

Furthermore, researchers should also consider the difference between aerobic and anaerobic exercise. According to the American Psychological Society, aerobic exercise is more likely to suppress appetite than anaerobic exercise. However, in a journal article by Broom et al., aerobic exercise did not influence ghrelin levels. This proves that the impact of exercise on ghrelin remains inconclusive for exercise type as well. For more consistent results, researchers must collect more varied data by altering their methodological design, such as altering the exercise prescription or training people for different periods of time.

#### Conclusion

In conclusion, the purpose of this paper was to inform the audience about the effects of exercise on the ghrelin hormone, and the biological and psychological processes that influence the effect of ghrelin on appetite. Based on the existing studies, exercise plays a crucial role in regulating ghrelin levels as ghrelin levels are highly dependent on body composition. More specifically, there was a general trend of increase in ghrelin levels following long-term chronic exercise and high-intensity exercise was more likely to suppress ghrelin than low-intensity exercise. It was also found that there were inconsistent results about the influence of acute exercise or exercise type (aerobic, anaerobic) on ghrelin.

Moving forward, it is important for researchers to conduct more studies with more diverse experimental designs in order to overcome the limitations of current findings. This would allow them to modify the experiments to reach a more consistent result. For instance, very few studies were found that explicitly contrasted aerobic and anaerobic exercise. Furthermore, it would be helpful for researchers to consider the different modalities within aerobic and anaerobic exercise such as comparing running and swimming or sprinting and weightlifting. Using this specific methodology may help scientists identify the contrasting physical impact of each type of physical activity on the body's hormonal response. By using these suggested methods, researchers may overcome the inconsistencies in current research and help people select the most appropriate type of exercise for the ghrelin response they want for their own purposes such as weight loss or gain.



# References

[1] Abizaid, A. (2009). Ghrelin and dopamine: new insights on the peripheral regulation of appetite. *Journal of neuroendocrinology*, *21*(9), 787-793.

[2] Al Massadi, O., Nogueiras, R., Dieguez, C., & Girault, J. A. (2019). Ghrelin and food reward. *Neuropharmacology*, *148*, 131-138.

[3] Arias-Carrión, O., & Pŏppel, E. (2007). Dopamine, learning, and reward-seeking behavior. *Acta neurobiologiae experimentalis*, 67(4), 481–488. <u>https://doi.org/10.55782/ane-2007-1664</u>

[4] Britannica, T. Editors of Encyclopaedia (2023, November 17). homeostasis. Encyclopedia Britannica. <u>https://www.britannica.com/science/homeostasis</u>

[5] Broom, D. R., Miyashita, M., Wasse, L. K., Pulsford, R., King, J. A., Thackray, A. E., & Stensel, D. J. (2017). Acute effect of exercise intensity and duration on acylated ghrelin and hunger in men. *Journal of Endocrinology*, *232*(3), 411-422.

[6] Broom, D. R., Stensel, D. J., Bishop, N. C., Burns, S. F., & Miyashita, M. (2007). Exercise-induced suppression of acylated ghrelin in humans. *Journal of applied physiology*, *102*(6), 2165-2171.

[7] Constantini, N., & Hackney, A. C. (Eds.). (2013). *Endocrinology of physical activity and sport* (pp. 437-53). New York: Humana Press.

[8] Davis, J., Camilleri, M., Eckert, D., Burton, D., Joyner, M., & Acosta, A. (2020). Physical activity is associated with accelerated gastric emptying and increased ghrelin in obesity. *Neurogastroenterology & Motility*, *32*(11), e13879.

[9] Deborah Anne Burton, Keith Stokes, George M Hall, Physiological effects of exercise, *Continuing Education in Anaesthesia Critical Care & Pain*, Volume 4, Issue 6, December 2004, Pages 185–188, https://doi.org/10.1093/bjaceaccp/mkh050

[10] Frecka, J. M., & Mattes, R. D. (2008). Possible entrainment of ghrelin to habitual meal patterns in humans. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *294*(3), G699-G707.

[11] Hackney, A. C., & Constantini, N. W. (Eds.). (2020). *Endocrinology of physical activity and sport*. Springer International Publishing AG.

[12] Kraemer RR, Castracane VD. Exercise and Humoral Mediators of Peripheral Energy Balance: Ghrelin and Adiponectin. Experimental Biology and Medicine. 2007;232(2):184-194. doi:10.3181/00379727-207-2320184

[13] Laviano, A., Molfino, A., Rianda, S., & Rossi Fanelli, F. (2012). The growth hormone secretagogue receptor (Ghs-R). *Current pharmaceutical design*, *18*(31), 4749–4754. <u>https://doi.org/10.2174/138161212803216906</u>

[14] Li, N., Li, N., Xu, F. *et al.* Selectively increasing GHS-R1a expression in dCA1 excitatory/inhibitory neurons have opposite effects on memory encoding. *Mol Brain* 14, 157 (2021). https://doi.org/10.1186/s13041-021-00866-8

[15] Merriam-Webster. (n.d.). Isoform. In Merriam-Webster.com dictionary. Retrieved December 19, 2023, from <u>https://www.merriam-webster.com/dictionary/isoform</u>

[16] Müller, T. D., Nogueiras, R., Andermann, M. L., Andrews, Z. B., Anker, S. D., Argente, J., ... & Tschöp, M. H. (2015). Ghrelin. *Molecular metabolism*, *4*(6), 437-460.

[17] Nwanne, Emerald. "Generational Wellness: Approaches to Weight Loss & Dieting." *Brightfield Group*,

https://blog.brightfieldgroup.com/generational-wellness-approaches-to-weight-loss-dieting. Accessed 13 Dec. 2023.

[18] Ouerghi, N., Feki, M., Bragazzi, N. L., Knechtle, B., Hill, L., Nikolaidis, P. T., & Bouassida, A. (2021). Ghrelin response to acute and chronic exercise: Insights and implications from a systematic review of the literature. *Sports medicine*, *51*(11), 2389-2410.

[19] Petrovich G. D. (2018). Lateral Hypothalamus as a Motivation-Cognition Interface in the Control of Feeding Behavior. *Frontiers in systems neuroscience*, *12*, 14. <u>https://doi.org/10.3389/fnsys.2018.00014</u>

[20] Rad, F. S., Haghparast, A., & Eliassi, A. (2020). Ventral Tegmental Area Microinjected-SKF38393 Increases Regular Chow Intake in 18 Hours Food-Deprived Rats. *Basic and Clinical Neuroscience*, *11*(6), 773.

[21] Rahman, M. S., Hossain, K. S., Das, S., Kundu, S., Adegoke, E. O., Rahman, M. A., Hannan, M. A., Uddin, M. J., & Pang, M. G. (2021). Role of Insulin in Health and Disease: An Update. *International journal of molecular sciences*, *22*(12), 6403. https://doi.org/10.3390/ijms22126403



[22] Schmidt, A., Maier, C., Schaller, G., Nowotny, P., Bayerle-Eder, M., Buranyi, B., ... & Wolzt, M. (2004). Acute exercise has no effect on ghrelin plasma concentrations. *Hormone and metabolic research*, *36*(03), 174-177.

[23] Sternson S. M. (2013). Hypothalamic survival circuits: blueprints for purposive behaviors. *Neuron*, 77(5), 810–824. <u>https://doi.org/10.1016/j.neuron.2013.02.018</u>

[24] Vatansever-Ozen, S., Tiryaki-Sonmez, G., Bugdayci, G., & Ozen, G. (2011). The effects of exercise on food intake and hunger: Relationship with acylated ghrelin and leptin. *Journal of sports science & medicine*, *10*(2), 283

[25] Yolanda Diz-Chaves, "Ghrelin, Appetite Regulation, and Food Reward: Interaction with Chronic Stress", *International Journal of Peptides*, vol. 2011, Article ID 898450, 11 pages, 2011. <u>https://doi.org/10.1155/2011/898450</u>