GLP-1 Use in Active Populations and Potential Effects on Glycogen Availability, Appetite, and Training Outcomes

Research Brief

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Abstract

Glucagon-like peptide-1 (GLP-1) receptor agonists have gained widespread clinical use for the management of type 2 diabetes and obesity due to their effects on glycemic control, appetite suppression, and weight loss. These agents prolong the short half-life of endogenous GLP-1, resulting in enhanced insulin secretion, reduced glucagon release, delayed gastric emptying, and altered central appetite regulation. While the metabolic and therapeutic benefits of GLP-1 receptor agonists are well established in clinical populations, their implications for athletic performance and recovery remain poorly understood. Emerging evidence suggests that GLP-1 receptor agonists may influence energy intake, substrate availability, and hormonal signaling related to satiety, raising concerns regarding adequate caloric and carbohydrate consumption in physically active individuals. Reduced carbohydrate intake may limit muscle glycogen availability, potentially impairing training quality, recovery, and overall performance. Comparisons with other substances known to alter metabolism in athletes, such as caffeine, clenbuterol, and thyroid hormones, highlight key differences in mechanisms and potential risks. Additionally, the growing off-label use of GLP-1 receptor agonists has introduced ethical, regulatory, and access-related challenges, particularly following their inclusion in the World Anti-Doping Agency monitoring program. Given the limited data available in athletic populations, further research is needed to evaluate the safety, metabolic consequences, and performance-related effects of GLP-1 receptor agonist use in high-performing individuals.

Key Words: Energy availability, Athletic performance, Glycogen metabolism.

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Introduction

Glucagon-like-peptide-1 (GLP-1) is a naturally occurring endocrine hormone in the gastrointestinal system that plays a role in blood sugar regulation, gastric emptying, and appetite suppression.[1] GLP-1 is secreted into the body after consuming food and attaches to GLP-1 receptors located in the pancreas, gastrointestinal tract, and brain.[2] According to studies the naturally occurring GLP-1 hormone degrades in the body within 1–2 minutes, however in 1991 Dr. John Eng found that extendin-4 peptide enabled drug development, leading to longer-acting agents, increasing the half-life up to five hours. Extendin-4 was later approved in 2005 as the first GLP-1 receptor agonist.[3] More recently in 2009–10 mechanisms used to increase GLP-1 half-life changed, targeting albumin binding and fatty acid side-chain modification which makes it more resistant to kidney filtration.[3] With these improvements the GLP-1 receptor agonist's half-life ranges from hours to days depending on the compound.

By increasing GLP-1's half-life in the body, through GLP-1 receptor agonist, the effects it has on the body can have a greater impact. This is why GLP-1 receptor agonists are often prescribed for type-2 diabetes and weight management. GLP-1's reduce blood glucose levels in the body by increasing insulin secretion. This is accomplished by targeting the beta cells in the pancreas, increasing their glucose sensitivity.[1] GLP-1's have an indirect effect on the delta cells in the pancreas that produce somatostatin. Somatostatin aids in decreasing glucagon secretion in alpha cells of the pancreas, causing a decrease in blood glucose levels. This proposes GLP-1 have an indirect effect on the alpha cells of the pancreas as well by inhibiting their secretion of glucagon.[1] Long term consequences of increased gastrointestinal hormone activity are still unknown as the majority of GLP-1 receptor agonist trials have been short-term.[2]

GLP-1 receptor agonist have a significant impact on insulin sensitivity and glucose production, but they are also thought to have an effect on metabolism and appetite suppression through the central nervous system.[4] Leptin, a hormone that signals to the brain that the stomach is full, is amplified by GLP-1 receptor agonist therefore suppressing hunger signals. GLP-1 receptor agonist can also cause nutrients in food to be absorbed slower which decreases gastric emptying.[4] This suggests a decrease in caloric intake when using GLP-1's which aids in weight loss. In a study consisting of eight male cyclists, it was found that leptin levels drop immediately after and up to two hours after exercise due to an energy deficit. At the end of exercise leptin dropped 21.4% and 60 minutes after exercising leptin dropped 21.2%.[5] This suggests that athletes using GLP-1 receptor agonists may experience stronger satiety signaling even when they are in an energy-deficit state. Normally, exercise reduces leptin concentrations following training due to acute energy expenditure, which helps stimulate appetite and refueling. However, GLP-1 agonists enhance central appetite suppression pathways, and it is currently unclear how these competing effects interact in athletes. This raises concern that athletes may feel adequately fueled despite insufficient caloric intake, which could negatively affect recovery and performance if not monitored appropriately. Supporting this concern, research on athletic nutritional behaviors shows that adequate caloric intake is essential for maintaining energy availability, supporting training demands, and promoting muscle healing and recovery.[6]

With a decrease in caloric intake, those using GLP-1 receptor agonist are also at risk for decreasing the amount of carbohydrates they consume. According to a study following a 3-day food intake survey among GLP-1 users the average carbohydrate intake was 184.6 grams. According to the Dietary Reference Intakes (DRI) the recommended intake is 275 grams of carbohydrates.[7] The decreased intake of carbohydrates would decrease glucose delivery to working muscles, therefore limiting glucose stores. During exercise the main source of energy in the body is blood glucose and a form of stored glucose called muscle glycogen. When these substrates are expended in the body athletes experience tiredness and weakness in the muscles.[8] If carbohydrates are used up the body moves to protein as a source of energy and decreases the amount of protein going to the muscles. This can reduce training quality in athletes as well as hinder recovery. Although limited research exists specifically in athletic populations, these concerns may be most relevant for endurance athletes, team-sport athletes with high training volumes, and athletes already at risk for low energy availability, where consistent carbohydrate intake is critical for maintaining performance and recovery.
While research on GLP-1 use in athletes is limited, there is extensive evidence regarding other substances used by athletes that influence body composition and metabolism. For example, stimulants such as caffeine can delay the onset of fatigue and enhance performance by blocking adenosine receptors in the central nervous system, which helps maintain alertness, reduce perceived effort, and support sustained exercise capacity.[9] Unlike GLP-1's, caffeine mainly targets the central nervous system increasing alertness and energy levels. Clenbuterol is a beta-agonist often misused among athletes as a performance-enhancing drug. Clenbuterol has many different effects on the body such as amplifying fat oxidation in individuals by increasing the amount of energy used to sustain basic bodily functions. However, glycogen levels in the muscles are not affected.[10] Another substance used among athletes are thyroid hormones. They are believed to help with weight loss while preserving muscle mass. Thyroid hormone supplements may be detrimental to both cardiovascular health and bone health if they are not used correctly.[11] Similar to clenbuterol, thyroid hormones increase metabolic rate and energy turnover, which can contribute to changes in body composition.[12]

Conclusion

Use of GLP-1 receptor agonists has become an increased scientific and public attention, bringing up many ethical and economical questions about the drug and how it is being used. Due to the attention brought to GLP-1's it has become popular to use the drug off-label for cosmetic purposes, creating a shortage that affects patients in need of the treatment.[13] With this shortage it may be difficult for athletes to access this drug or if they have been using it, they may not want to speak on their experience using it, hence the lack of research with this population. Another reason athletes may be hesitant to speak out about their GLP-1 use is because the World Anti-Doping Agency added GLP-1 receptor

agonists to the WADA monitoring program in 2024, however it is not yet on the WADA prohibited list.[14] With this and the potential adverse effects for GLP-1 receptor agonists such as decreased energy intake, impaired recovery, and reduced muscle performance, athletes may not view GLP-1's as a performance enhancing drug. More research on this population of highly performing individuals is needed to ensure safe and responsible use.

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None

Conflict of Interest
None

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