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GLP-1 Agonists Reimagined: The Tripartite Applications of the Semaglutide Hormone

Joon Daniel Park [1], Merajur Rahman [2], Jeffrey Ye[3]

[1]Northern Valley Regional High School at Old Tappan, 100 Central Ave, Old Tappan, NJ 07675, United States
[2]The Bronx High School of Science, 75 W 205th St, Bronx, NY 10468, United States
[3]Francis Lewis High School, 58-20 Utopia Pkwy, Fresh Meadows, NY 11365, United States

Abstract

Semaglutide, a GLP-1 receptor agonist has been initially adopted as a treatment and regulator for the Type 2 Diabetes disease. In this essay, we will be focusing on the three primary roles that the semaglutide fulfills throughout day to day life or in potential real world applications. We examined different hormones related to the endocrine system, and identified differences in weaknesses and strengths between GLP-1 and semaglutide. We also assessed the different roles that semaglutide may be used for. The original intended use being Type 2 Diabetes regulation, where we established the utilization of the potent insulin releasing trait of semaglutide being the key factor for Type 2 Diabetes regulation. A repurposed use for weight reduction, where we identified the secondary symptoms of insulin release such as lower appetite. Finally, a speculative application where the diabetes regulation capabilities may have a positive correlation in affecting neurological diseases such as dementia. Through the compilation and review of historic and recent sources, this paper highlights the broader usage of the semaglutide compound. The findings suggest that semaglutide's mechanisms and variety makes it a promising candidate for future metabolic and potentially groundbreaking neurological medicine.

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Ozempic, utilized by people of all body types, is a wonder drug in the diabetes regulation industry. But how efficient and effective is the drug? Ozempic, a prescription medicine—whose active compound is semaglutide— has been primarily given to people with Type 2 diabetes. Although Semaglutide has been used exclusively for diabetes during its period of relevance, it has also been prescribed for weight loss; specifically for people with a Body Mass Index (BMI) of 27-30 (Ozempic, 2024). A BMI of 27-30 signifying that an individual is overweight and is susceptible to many associated health complications (Zierle-Ghosh & Jan, 2023). Although its primary use remains as a diabetes management option, semaglutide's

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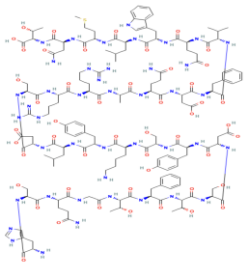
broader therapeutic potential has sparked widespread interest and use, with some of its additional applications still under active investigation.

GLUCAGON and GLP-1

The Glucagon-like Peptide-1 (GLP-1) is a naturally occurring hormone that is found in the inner linings of the large and small intestines of the human body (Cabou, 2011). Semaglutide is a synthetic compound sharing similar chemical constructs and traits of GLP-1 (Mahapatra & Karuppasamy et al, 2022). The GLP-1 and glucagon hormones derive from precursor protein preproglucagon, all of which are responsible for the bodily regulation of glucose, digestive functions, and appetite (Landgraf & Neumann et al, 2017). GLP-1's specific task is to lower the blood sugar level by releasing insulin. GLP-1 works in a complementary fashion with its other hormonal counterpart, Glucagon, which increases the blood sugar level in the body. Both Glucagon and GLP-1 work together to maintain the balance of the glucose in the body, where both are released depending on how low or high the blood sugar is. While preproglucagon is produced in various parts of the body, including the pancreas and intestines, its derivatives – such as Glucagon and GLP-1 are synthesized by different specialized cells (Whalley & Pritchard et al, 2011).

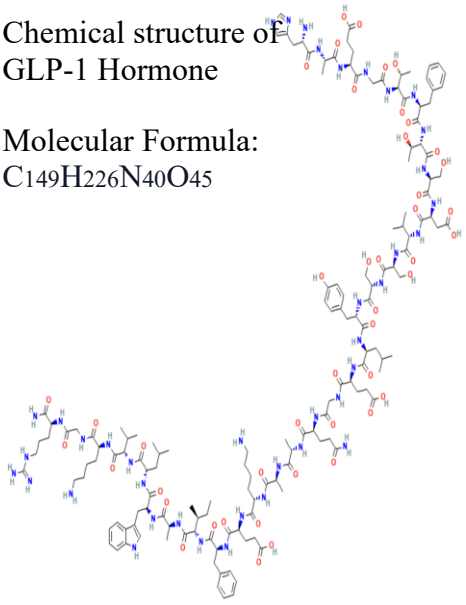


Glucagon Molecular Structure

National Center for Biotechnology

Chemical structure of GLP-1 Hormone

Molecular Formula: $C_{149}H_{226}N_{40}O_{45}$



National Center for Biotechnology Information. (n.d.). *Glucagon-like peptide-1(7-36) amide*. PubChem Compound Summary for CID 16133797. Retrieved July 18, 2025, from https://pubchem.ncbi.nlm.nih.gov/compound/Glucagon-like-peptide-1_7-36_-amide

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Glucagon, the hormone that increases glucose levels, is usually produced and stored in the pancreatic α cells, which are cells specifically evolved to convert preproglucagon to glucagon hormones. GLP-1 on the other hand is usually produced by the intestinal L-cells which are of similar role to the pancreatic α cells in which the intestinal L-cells produce GLP-1. However, unlike the Glucagon/pancreatic α cell relationship of storage, the GLP-1/ intestinal L-cells do not have a storage system but are secreted quickly when sustenance starts to enter the bodily system. As GLP-1 arrives at the pancreas, the hormones attach to their respective receptors called the GLP-1 Receptors (GLP1R) activate a messenger enzyme called the adenylate cyclase (Drucker, 2018). The adenylate cyclase then converts adenosine triphosphate (the main energy currency ATP) into cyclic adenosine monophosphate (cAMP), a secondary messenger within the signaling pathway. Only through the cAMP are the protein kinase A (PKA) and the guanine exchange factor protein (ie RAPGEF4 or Epac2) allows calcium to trigger the β cells in the pancreas to release the insulin. Similarly to the pancreatic α cell and glucagon system, the pancreatic β cell produces insulin and stores them inside itself, through the usage of a vesicle. These vesicles provide protection and containment of the insulin hormone. To release insulin, the vesicles gently fuse with the beta cell membrane to release insulin gradually through the cell wall. Through insulin, all of the aforementioned therapeutic traits are exhibited; such as lack of appetite, the regulation of glucose, and suppression of glucagon secretion(Woods & Lutz et al, 2006).

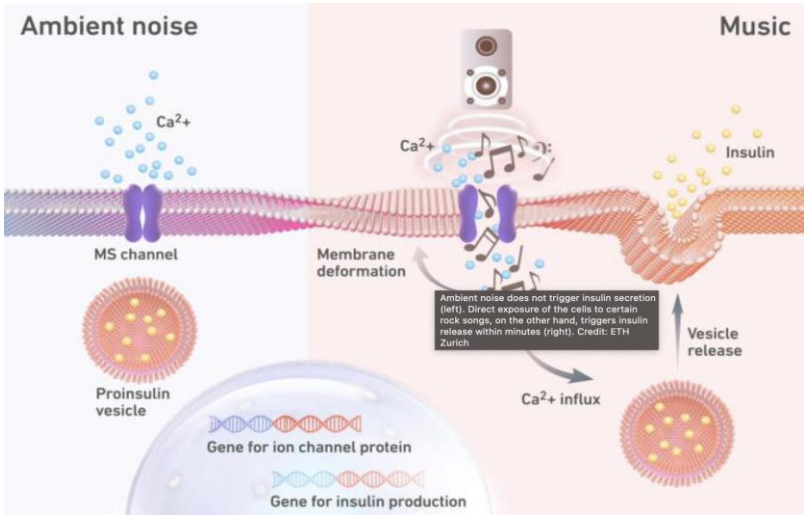

Photo Left: Shows the insulin releasing process with the Calciu

Temple University Health System. (2023, August 16). *Gene*

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GLP-1 was discovered by Jens Juul Holst and Joel Habener GLP-1 in the 1970s, and was originally thought to have been related to stomach ulcer occurrence in the human body (Reynolds. 2023). Despite its original inception, through further tests it was found to be naturally secreted during food consumption, leading to the first correct understanding of GLP-1. By the 1990s, GLP-1 was being studied and modified for its therapeutic potential in treating insulin-related issues in diabetes, most notably by Michael A. Nauck, eventually creating the artificial analog hormone semaglutide (Media Centre). His research was later sponsored by the pharmaceutical company Novo Nordisk to further explore its applications. It took nearly 30 years after the discovery of GLP-1 before the semaglutide was introduced to the public as a diabetes treatment under the name Ozempic.

While semaglutide shares around 94% of its chemical makeup with GLP-1, there are a couple differences in its structure that yield vastly different properties. The first of the three major differences is that semaglutide does not have an alanine in position 8 rather an alpha-aminoisobutyric acid (Aib). Aib is a non-proteinogenic amino acid — an amino acid that is not associated with the 22 proteinogenic amino acids — that is most commonly developed in a lab (Friedman, 2024). The GLP-1's main factor of its brevity has been accredited to its vulnerability to dipeptidyl peptidase-4 (DPP-4), an enzyme that specifically targets the 8th alanine (Ala) in GLP-1(Knudsen & Lau, 2019). The DPP-4 enzyme cleaves the GLP-1 hormone, drastically contributing to its very short half life span to around 1-2 minutes. Additionally because GLP-1 has been cleaved it renders the hormone ineffective in releasing insulin as the receptors become unresponsive to the cut GLP-1 hormone (Drucker, 2006). By replacing the Ala residue with the Aib acid, GLP-1 essentially becomes "immune" to the DPP-4 enzyme, in turn allowing it to have a longer half-life span (Friedman, 2024). The second major difference is the Fatty Acid Attachment. While there is no replacement of Amino Acids in the second major difference, an additional compound called Octadecanedioic acid (simply known as C18 diacid) is bonded to the side chain of Lysine 26 (FDA, 2017). Similarly to the function, the Octadeconedioic acid extends the half life of GLP-1, albeit in a different fashion (Lau & Block et al, 2015). Contrarily to increasing immunity to the GLP-1 decomposers, the C18 diacid binds to the protein Albumin which is located in the blood vessels. By leveraging the hydrophobic properties of the protein, semaglutide is protected by essentially hiding away from a large majority of its degraders, such as the liver, DPP-4 enzymes, and other metabolic networks. The last major difference between semaglutide and GLP-1 is the 34 amino acid position. Originally lysine (Leu) it is replaced with arginine (Arg) to make the hormone more stable. GLP-1 is already unstable in the body, and is evidently so because of the 1-2 minute half life. Through the lysine change on position 34, the semaglutide is less susceptible to chemical acylations, leading to a higher half life span of roughly 1 week. Through these three primary modifications, semaglutide lends itself as a potent and efficient hormone compared to the naturally occurring GLP-1 (Lau & Block et al, 2015). Through these traits, semaglutide is

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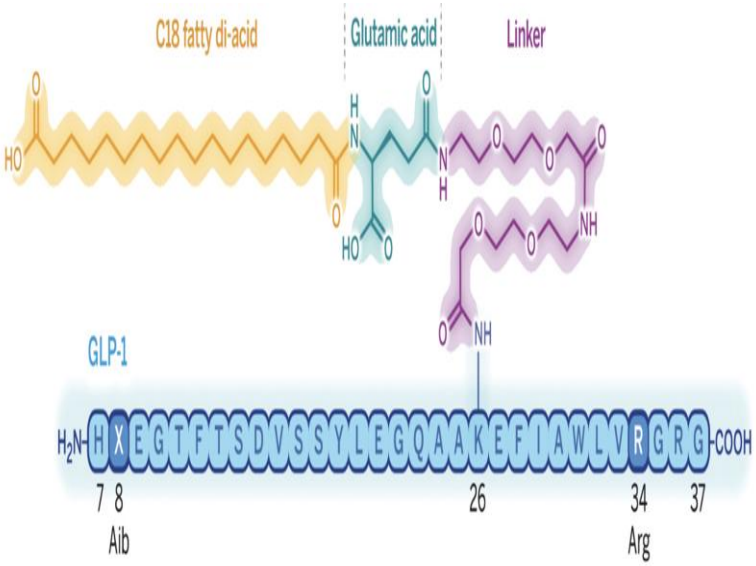
able to release more insulin at a faster rate, leading to its therapeutic properties exhibited throughout the body.



Habtemichael, E. N., Qu, L., Verma, S., Soleimani, M., Chiang, S. H., & Saltiel, A. R. (2024). A neuronal circuit that inhibits the brain's control of insulin secretion and glucose metabolism. *Proceedings of the National Academy of Sciences, 121*(30), e2415550121.

Image Left: Alanine 8, marked by an x is replaced by Aid Acid as shown in graphic. Top chain of molecules represents the C18 fatty di-acid module adhering to Lysine 26 Leucine 34 replaced by Arginine

While small changes may yield vastly different outcomes for many proteins, semaglutide still manages to accomplish the position GLP-1 usually accomplishes through two main factors. Semaglutide can still bind to the GLP-1 receptor because its N-terminal remains identical to that of natural GLP-1, which is the region responsible for receptor attachment. The other factor of semaglutide being able to bond to its receptor is that it is still able to retain a similar shape. GLP1R is considered a G protein coupled receptor (GPCR), which is a category of receptors that identifies and allows hormones to bond with it based on the three dimensional shape rather than the chemical makeup of the hormone. All in all, while semaglutide has significant modifications that allows it to be more potent compared to its naturally occurring counterpart, it still retains its general identity which allows it to have its agonist properties.

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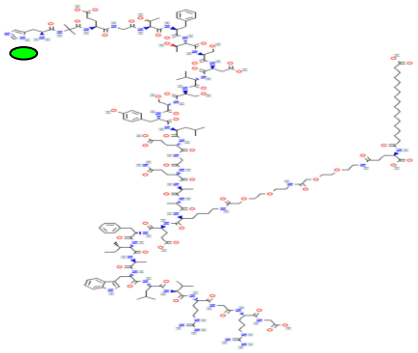
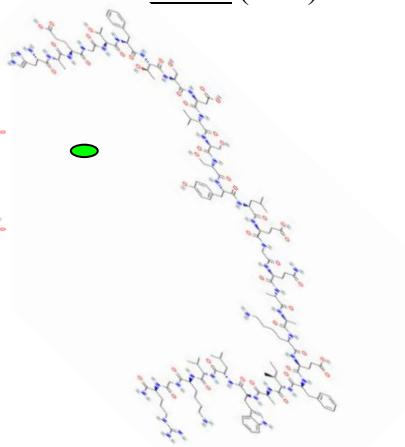
Treatments for Diabetes

While semaglutide is not usually prescribed as the first line of treatment for type 2 diabetes, its efficiency in releasing insulin in the body has been one of the primary reasons as to why the drug has been so prevalent. Type 2 diabetes (T2D) is a chronic condition that affects the



National Center for Biotechnology Information. (n.d.). *Semaglutide*. PubChem Compound Summary for CID 56843331. Retrieved July 18, 2025, from



National Center for Biotechnology Information. (n.d.). *Glucagon-like peptide-1(7-36) amide*. PubChem Compound Summary for CID 16133797. Retrieved July 18, 2025, from https://pubchem.ncbi.nlm.nih.gov/compound/Gluca

Semaglutide - left
GLP-1 - Right

The N-terminals (start of the N

body by reducing insulin level in the body (American Diabetes Association, 2024). As previously mentioned, insulin's primary role in the human body is to lower excess glucose levels in the blood when it becomes elevated. When an individual has T2D, the Glucagon level usually rises and GLP-1 levels decrease in response to digesting food. Because of the lack of insulin releasers, less insulin is released into the circulatory system, leading to excess glucose in the circulatory system. Hyperglycemia, when the glucose level in the circulatory system is too high can lead to a variety of health complications such as the kidneys, eyes, brain, nerves, heart, etc(Clevel and Clinic, 2023) Through the disruption in the bodily glucose level, the body will cease to function and in worse case, may die. Semaglutide, when injected, provides the body with extra GLP-1 that are more potent and longer lasting, allowing the body to produce the insulin it needs to retain its balance. While other medications have been utilized, semaglutide (Ozempic), is a particularly exceptional drug that can be utilized for T2D. For one, Ozempic has been known for its semaglutide injection method rather than oral medication. Semaglutide Injection has been particularly more efficient in regulating glucose levels because it allows the hormones to directly enter the blood stream. By completely avoiding the

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gastrointestinal system, which is a particularly harsh system of the human body, the semaglutide is able to stay more potent and longer lasting compared to other methods of administration. Moreover, because semaglutide is still an amino acid, it can render the hormone useless as the human stomach acid's primary function is to break them apart (Dix, 2021). While semaglutide is used to treat diabetes, the drug's diverse therapeutic properties have sparked growing interest in its potential applications for other health conditions such as weight loss.

Weight Loss for Obesity

Semaglutide which was originally utilized as a treatment for type 2 diabetes was recently repurposed for additional medical uses due to its effects on glucose metabolism and appetite suppression. Recent clinical trials have shown that patients lost around 15% of body weight on average and even reported reduced binge eating and fewer cravings (Garvey & Batterham et al, 2022). Obesity and being overweight are symptoms of many underlying diseases such as diabetes and cancer. Utilizing the Body Mass index individuals can be generalized into either being underweight, normal weight, or overweight, and in extreme cases, obese. At the BMI range of 25.0 - 29.9 individuals are classified as overweight, considered to be Class 1 Obese when at 30.0 - 34.9, Class 2 Obese when at 35.0 - 39.9, and Morbidly Obese when BMI is greater than or equal to 40.0 (Aim for a Healthy Weight, n.d.). While obesity is its standalone disease, it can also be symptoms for T2D and many other health complications. Some symptoms that may be caused by obesity is Hypertension (high blood pressure) which can damage blood vessels and arteries which can slowly degrading the body;

WEIGHT	lbs	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270	280	290
	kgs	41	45	50	54	59	64	68	73	77	82	86	91	95	100	104	109	113	118	122	127	132
HEIGHT			Underweight					Healthy				Overweight				Obese				Extremely Obese		
ft/in	cm																					
4'8"	142.2	20	22	25	27	29	31	34	36	38	40	43	45	47	49	52	54	56	58	61	63	65
4'9"	144.7	19	22	24	26	28	30	32	35	37	39	41	43	45	48	50	52	54	56	58	61	63
4'10"	147.3	19	21	23	25	27	29	31	33	36	38	40	42	44	46	48	50	52	54	56	59	61
4'11"	149.8	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	51	53	55	57	59
4'12"	152.4	18	20	21	23	25	27	29	31	33	35	37	39	41	43	45	47	49	51	53	55	57
5'1"	154.9	17	19	21	23	25	26	28	30	32	34	36	38	40	42	43	45	47	49	51	53	55
5'2"	157.4	16	18	20	22	24	26	27	29	31	33	35	37	38	40	42	44	46	48	49	51	53
5'3"	160.0	16	18	19	21	23	25	27	28	30	32	34	35	37	39	41	43	44	46	48	50	51
5'4"	162.5	15	17	19	21	22	24	26	27	29	31	33	34	36	38	39	41	43	45	46	48	50
5'5"	165.1	15	17	18	20	22	23	25	27	28	30	32	33	35	37	38	40	42	43	45	47	48
5'6"	167.6	15	16	18	19	21	23	24	26	27	29	31	32	34	36	37	39	40	42	44	45	47
5'7"	170.1	14	16	17	19	20	22	24	25	27	28	30	31	33	34	36	38	39	41	42	44	45
5'8"	172.7	14	15	17	18	20	21	23	24	26	27	29	30	32	33	35	37	38	40	41	43	44
5'9"	175.2	13	15	16	18	19	21	22	24	25	27	28	30	31	33	34	35	37	38	40	41	43
5'10"	177.8	13	14	16	17	19	20	22	23	24	26	27	29	30	32	33	34	36	37	39	40	42
5'11"	180.3	13	14	15	17	18	20	21	22	24	25	27	28	29	31	32	33	35	36	38	39	40
5'12"	182.8	12	14	15	16	18	19	20	22	23	24	26	27	28	30	31	33	34	35	37	38	39
6'1"	185.4	12	13	15	16	17	18	20	21	22	24	25	26	28	29	30	32	33	34	36	37	38
6'2"	187.9	12	13	14	15	17	18	19	21	22	23	24	26	27	28	30	31	32	33	35	36	37
6'3"	190.5	11	13	14	15	16	18	19	20	21	23	24	25	26	28	29	30	31	33	34	35	36
6'4"	193.0	11	12	13	15	16	17	18	19	21	22	23	24	26	27	28	29	30	32	33	34	35
6'5"	195.5	11	12	13	14	15	17	18	19	20	21	23	24	25	26	27	28	30	31	32	33	34
6'6"	198.1	10	12	13	14	15	16	17	18	20	21	22	23	24	25	27	28	29	30	31	32	34
6'7"	200.6	10	11	12	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	32	33
6'8"	203.2	10	11	12	13	14	15	16	18	19	20	21	22	23	24	25	26	27	29	30	31	32
6'9"	205.7	10	11	12	13	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	31
6'10"	208.2	9	10	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
6'11"	210.8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	25	26	27	28	29	30

Houston Weight Loss Center. (n.d.). *Body mass index*.

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High cholesterol, where plaque in the arteries may start to build up; and many other health problems that usually affects day to day life and in severe cases lead to death (Atherosclerosis, n.d.). The most important trait that allows semaglutide to be used as a weight loss supplement is that it affects the Central Nervous system, where there are GLP-1 receptors such as the Vagal Afferent Nerves and Enteric Neurons. Vagal Afferent Nerves' primary function being sending information from the gut to the brain, which additionally controls the majority of the involuntary body functions such as: digestion, heart rate, and immune system. Enteric Neurons are embedded in the walls of the gastrointestinal tract and are responsible for the coordination of digestion and emotional balance; main focus being digestion suppression (Furness, 2012).

Evidently, semaglutide intake can lead to relaxation of the lower parts of the stomach or precisely the Antrum and pylorus, reducing contractions and slowing the movement of food from the stomach, or through the process known as Gastric Motility Inhibition (GMI). Through these key differences it allows the body to react differently, giving it the weight loss properties for obesity (Drucker, 2018). As food is in the body for a longer period of time, individuals may feel more full, leading to less food in the body. Due to the fact that the glucose absorption is slower than without the use of semaglutide, it reduces post meal blood sugar spikes. While these two health conditions remain the only FDA-approved uses of the drug, there are also strides in speculative applications, including potential benefits for conditions such as dementia.

Downsides to Semaglutide

However, while semaglutide has its strengths it is without its flaws. Upon injecting semaglutide into the body, it has been proven that individuals may experience: Nausea, Vomiting, Diarrhea, Constipation, Abdominal pain, and fatigue (Ozempic, Novo Nordisk). While these side effects are common during early phases of semaglutide usage, they may persist. Moreover, through the usage of semaglutide people may be more susceptible to pancreatitis, the inflammation of the pancreas, because they may be experiencing more stress than normal because of heightened insulin release (Nauck et al, 2013). Moreover, gallbladder issues such as gallstones and gallbladder inflammation may be more susceptible because of delays in gallbladder emptying. Stagnant bile in the gallbladder may contribute to cholesterol crystals forming, which are the leading cause of gallstones (Wilding, 2021). The primary drawback for semaglutide is the rapid weight loss properties itself. As individuals are less susceptible to change, rapid dietary changes may leave no time for individuals to develop healthy lifestyles such as dietary changes and ability to exercise. Without the necessary lifestyle changes, individuals are more likely to gain back a lot of the weight(Wu & Yang et al, 2025). Rapid and major weight fluctuations may lead to a plethora of health issues such as cardiovascular risks, and disruption in mental health. One major drawback to semaglutide injections is the suspected increase in thyroid cancer. After injecting rats with semaglutide, it has been suspected it causes an increase in thyroid cancer. However, while these issues may

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persist in rats, it is still too early to assume the same can be applied for humans. Therefore it is important to inform the prescriber for any familial history pertaining to thyroid cancer (Medline Plus, n.d.).

DEMENTIA AND NEUROLOGICAL ASPECTS

The interest in semaglutide's neurological effects stems from its ability to modulate pathways that are disrupted in neurodegenerative and neuropsychiatric disorders. Alzheimer's disease and other forms of dementia are characterized by chronic neuroinflammation, oxidative stress, mitochondrial dysfunction, and impaired glucose metabolism in neurons. These pathological processes lead to the accumulation of toxic amyloid-beta plaques (Aβ Plaques) and tau tangles, causing progressive cognitive decline. Derived from the amyloid precursor protein (APP), a diverse functioning protein specifically related to the nervous system, Amyloid-beta plaques are sticky faulty protein fragments that build up outside of the neurons. Due to the fact that Aβ plaques are blocking the neurons from transmitting information to the main body system, they play a key role in Alzheimer's and other neurodegenerative diseases (Selkoe & Hardy, 2016). Similarly to Aβ plaques, Tau tangles are also known to build up outside the neurons preventing information relay. The protein tau primarily stabilizes microtubules, which are akin to supply lines that provide nutrients, proteins and a variety of other essential resources to the brain. When a tau protein becomes abnormally hyperphosphorylated, meaning the protein is carrying too many phosphate groups, it starts to detach from the microtubules and starts to misfold and adhere to itself. This self adhesion leads to a large blockage in the microtubules that prevents proteins and a variety of other essential resources from entering the brain(Wang & Mandelkow, 2016). Semaglutide, by activating GLP-1 receptors in the brain, triggers signaling cascades such as the PI3K/Akt pathway, which serves as an enzyme that gets activated to regulate cell growth, survival, proliferation, and metabolism(Manning & Toker, 2017). that promote neuronal survival and enhance synaptic plasticity. In animal models of Alzheimer's, GLP-1 receptor agonists have been shown to reduce amyloid-beta accumulation, suppress microglial overactivation (which drives inflammation), and restore neuronal glucose uptake, thereby improving cognitive performance (Gejl et al., 2016). Early human studies support these findings; in a six-month randomized controlled trial, semaglutide preserved brain glucose metabolism in Alzheimer's patients, suggesting a potential disease-modifying effect rather than merely symptomatic relief. Building on these results, a larger clinical trial (NCT04777396) is currently investigating whether semaglutide can slow cognitive decline in patients with early Alzheimer's disease.

Semaglutide demonstrates neurological advantages that extend beyond its potential to treat Alzheimer's disease. The underlying mechanisms of vascular dementia and other forms of dementia include chronic inflammation and metabolic dysfunction which GLP-1 receptor activation can help to reduce. The therapeutic potential of semaglutide extends to Parkinson's disease which represents another major neurodegenerative disorder. Parkinson's disease develops when the substantia nigra, a midpoint brain component that initiates and coordinates

Technium BioChemMed Vol. 13, pp.212-226 (2025)
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body movement, loses its dopamine-producing neurons progressively which results in tremors and motor impairment and stiffness (Substantia nigra, 2011). The degeneration of neurons in Parkinson's disease is primarily caused by mitochondrial dysfunction and neuroinflammatory processes. Preclinical studies demonstrate that GLP-1 agonists protect dopaminergic neurons and decrease oxidative damage while enhancing motor function which positions semaglutide as a promising Parkinson's disease treatment (Marucci et al., 2023). The neuroprotective effects observed with exenatide in human trials support further research of semaglutide as a potential treatment for Parkinson's disease.
The neurological applications of semaglutide reaches beyond traditional neurodegenerative conditions to include behavioral and psychiatric disorders. The reward system of the brain through its mesolimbic dopamine pathway, a major dopamine conductor to the brain, functions as a primary mechanism for addiction. The GLP-1 receptors in this circuit determine how the brain processes rewarding stimuli including alcohol and nicotine and opioids. Research with rodents demonstrates that GLP-1 receptor agonists both minimize the pleasurable aspects of addictive substances and lower drug-seeking behaviors. The GLP-1 agonist semaglutide shows promise for treating alcohol use disorder because diabetic patients who take this medication report decreased alcohol cravings and reduced drinking habits (Holst et al., 2021). Research into semaglutide's potential treatment of substance use disorders including opioid and cocaine addiction has gained momentum because these conditions involve dopamine signaling dysregulation. The ability of semaglutide to normalize reward processing makes it a promising non-addictive treatment for addiction management.

The medication may also affect other psychiatric disorders that involve impulse control and cognitive regulation. Tying back to the aforementioned therapeutic properties, semaglutide has the potential to improve executive function and decision-making abilities because it enhances brain insulin sensitivity and energy metabolism which are typically impaired in binge eating disorder and compulsive overeating. The GLP-1 receptors which control satiety and hunger signals allow semaglutide to decrease food consumption through metabolic means while simultaneously affecting brain food-seeking behavior albeit in an addictive manner. Research indicates that semaglutide has the potential to connect metabolic diseases with psychiatric conditions by providing a unified treatment strategy for disorders affecting both physical and behavioral aspects.

The neurological application of semaglutide demonstrates an essential medical transformation which shows that metabolic wellness and brain wellness form an inseparable connection. Medical professionals have named Alzheimer's disease "type 3 diabetes" because the brain develops insulin resistance. Semaglutide works by enhancing glucose metabolism and decreasing inflammation which targets the same mechanisms that contribute to diabetes and neurodegenerative diseases. The dual therapeutic properties of this medication position it as an exceptional treatment option which can help slow disease progression while sustaining overall body health. The practical benefits of drug repurposing

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become evident when using semaglutide. The FDA has already approved semaglutide for diabetes and obesity treatment so its safety profile and manufacturing processes and pharmacokinetics are already established which shortens the time needed for clinical development in neurological applications.

The adoption of semaglutide as a neurological treatment faces multiple obstacles before it can become widely available. The main obstacle to semaglutide's use in brain tissue is its limited ability to pass through the blood–brain barrier. Scientists are working on two approaches to enhance semaglutide's central nervous system penetration: developing new versions of the drug and using nanoparticles as delivery systems. The promising results from preclinical and early clinical studies need to be confirmed through larger and longer-term trials to determine semaglutide's ability to stop or slow neurodegenerative disease progression. The expanding evidence indicates semaglutide functions as an innovative example of how metabolic disorder medications can be transformed into neurological disease treatments.

The neurological applications of semaglutide demonstrate great potential to revolutionize treatment methods for Alzheimer's disease as well as broader dementia syndromes and Parkinson's disease and substance use disorders. Semaglutide targets brain GLP-1 receptors to decrease neuroinflammation while enhancing neuronal energy metabolism and protecting vulnerable neurons and regulating reward pathways. The ongoing clinical trials have the potential to validate semaglutide's effects which would establish it as a first metabolic therapy to deliver significant neurological advantages between two distinct medical fields while providing hope to patients with currently untreatable conditions.

Semaglutide exemplifies how modern pharmacology can reimagine naturally occurring hormones into potent, long-lasting therapeutics. Initially developed as a treatment for Type 2 diabetes, semaglutide’s effectiveness stems from strategic modifications that enhance the naturally occurring GLP-1’s stability, bioavailability, and receptor affinity: allowing for sustained release of insulin, improved glucose control, and appetite suppression. These properties have enabled its repurposing for weight management, offering a therapeutic solution for individuals affected by obesity and other related metabolic disorders.

Yet semaglutide’s influence reaches far beyond metabolic regulation. Emerging evidence suggests that GLP-1 receptor activation has protective effects in the central nervous system, including reduced neuroinflammation, enhanced synaptic function, and improved neuronal glucose metabolism. These findings have led to promising investigations into semaglutide’s role in treating neurodegenerative diseases such as Alzheimer’s and Parkinson’s. In Alzheimer’s models, semaglutide has been shown to reduce amyloid-beta plaque and tau tangle accumulation.

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A new hypothesis proposes a dual-action model: that semaglutide not only activates protective cellular pathways but may also interact directly with amyloid-beta and tau aggregates. This concept, though still underexplored, could be investigated using in silico molecular docking (ISM), a computational method that simulates how semaglutide might bind to fibrillar forms of these proteins.

Altogether, semaglutide's wide-ranging therapeutic potential—from managing glucose and body weight to possibly altering the course of Alzheimer's disease—demonstrates the transformative power of drug repurposing. It bridges the gap between metabolic and neurological health, prompting a re-evaluation of how hormonal signaling pathways can be harnessed for conditions once thought to be unrelated. As research advances, semaglutide may serve as a blueprint for future multi-functional drugs that transcend their original medical purpose and open doors to new treatments across disciplines.

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