

Amylin

Effects on glucose metabolism

START

BACK

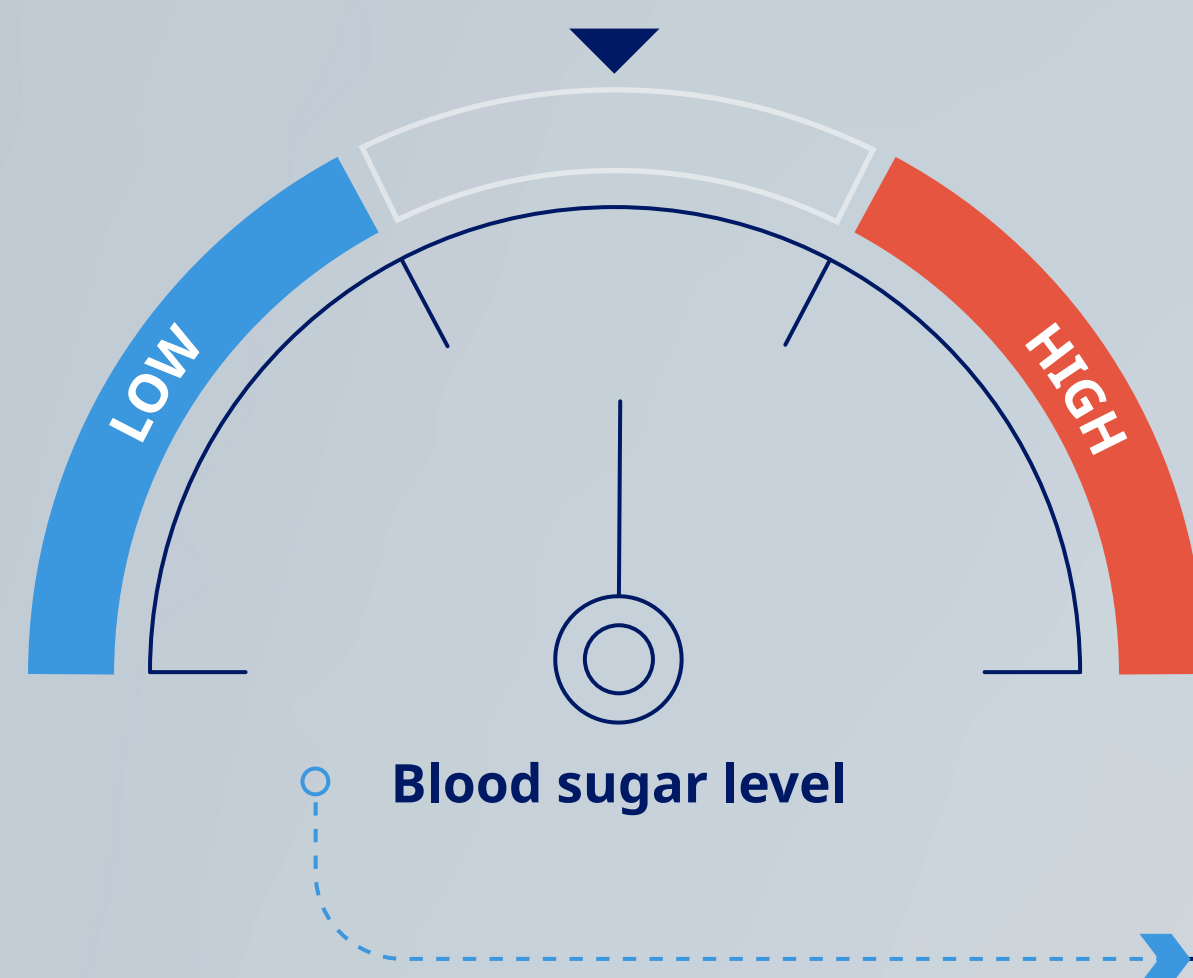
Welcome to our exploration of amylin and its effects on glucose metabolism. Join us as we delve into the multifaceted roles of this hormone, uncovering the mechanisms that impact glucose metabolism

NEXT

[BACK](#)

The importance of regulating postprandial hyperglycemia

Please click either 'low' or 'high' on the dial to see how glucose levels affect the body



Before we explore the effects of amylin on glucose metabolism, let us first dive into the importance of postprandial glucose control

Excessive postprandial glucose excursions, alongside basal hyperglycemia, contribute to the overall elevations in HbA_{1c} levels seen in people with diabetes¹

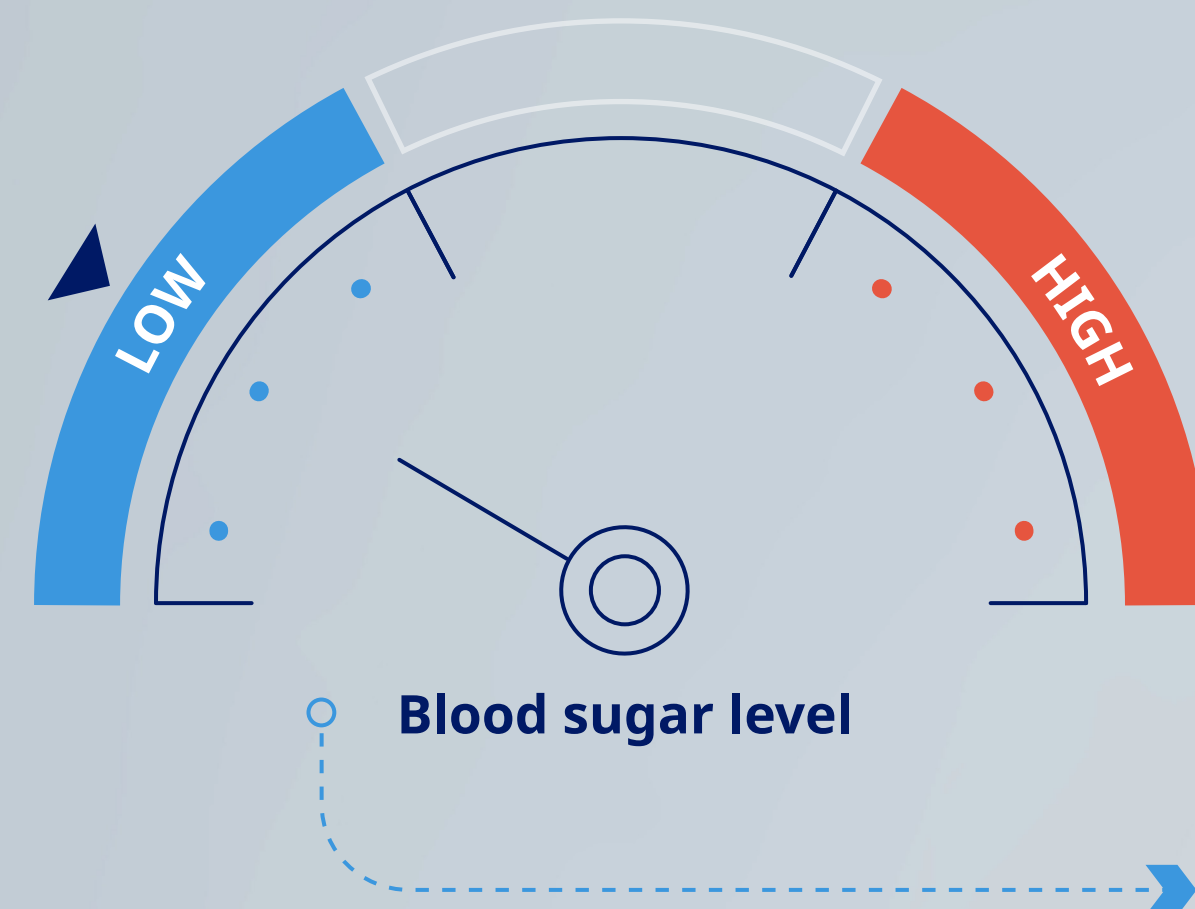
Restoring postprandial glucose homeostasis is key to achieving satisfactory glycemic control¹

[NEXT](#)
[REFERENCES](#)

[BACK](#)

The importance of regulating postprandial hyperglycemia

Please click either 'low' or 'high' on the dial to see how glucose levels affect the body



Blood sugar level

In healthy people, fasting plasma glucose concentration is tightly controlled within a narrow range¹

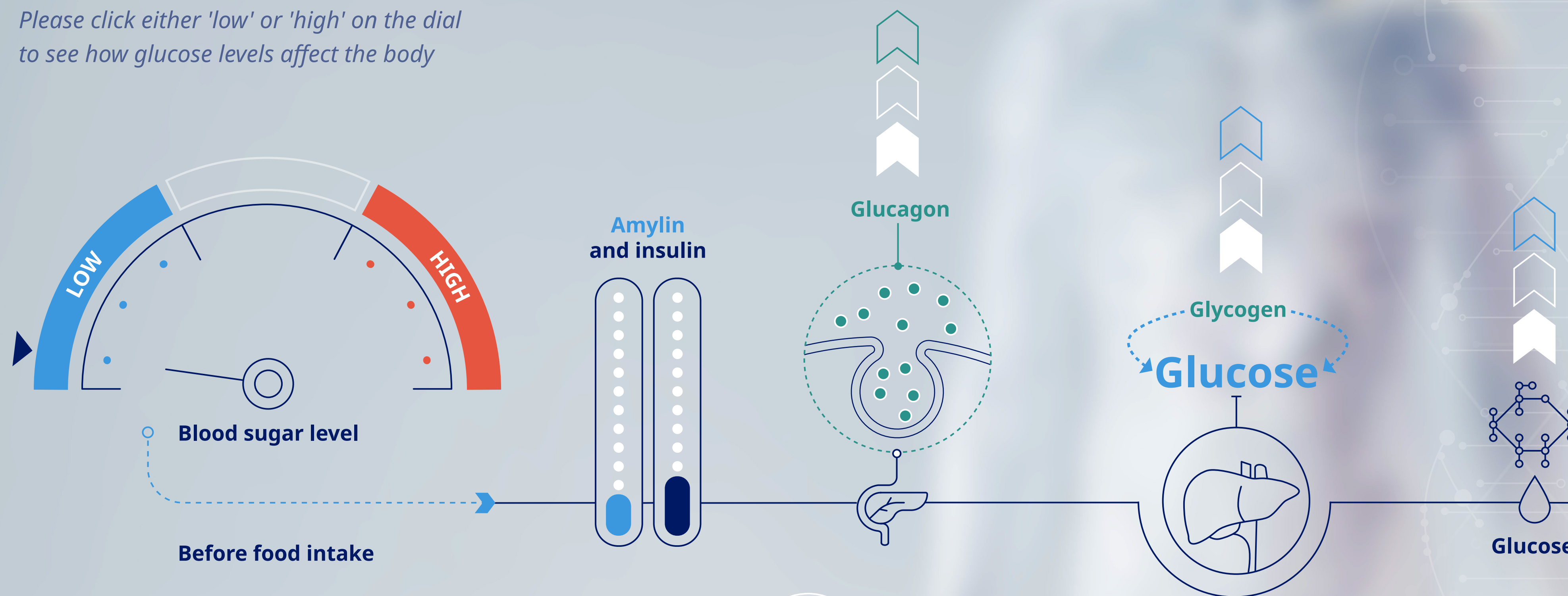
During fasting, decreased blood glucose levels trigger glucagon secretion from pancreatic α cells¹

This helps maintain energy by increasing glucose levels, which is achieved by breaking down glycogen into glucose in the liver¹

[NEXT](#)[REFERENCES](#)

The importance of regulating postprandial hyperglycemia

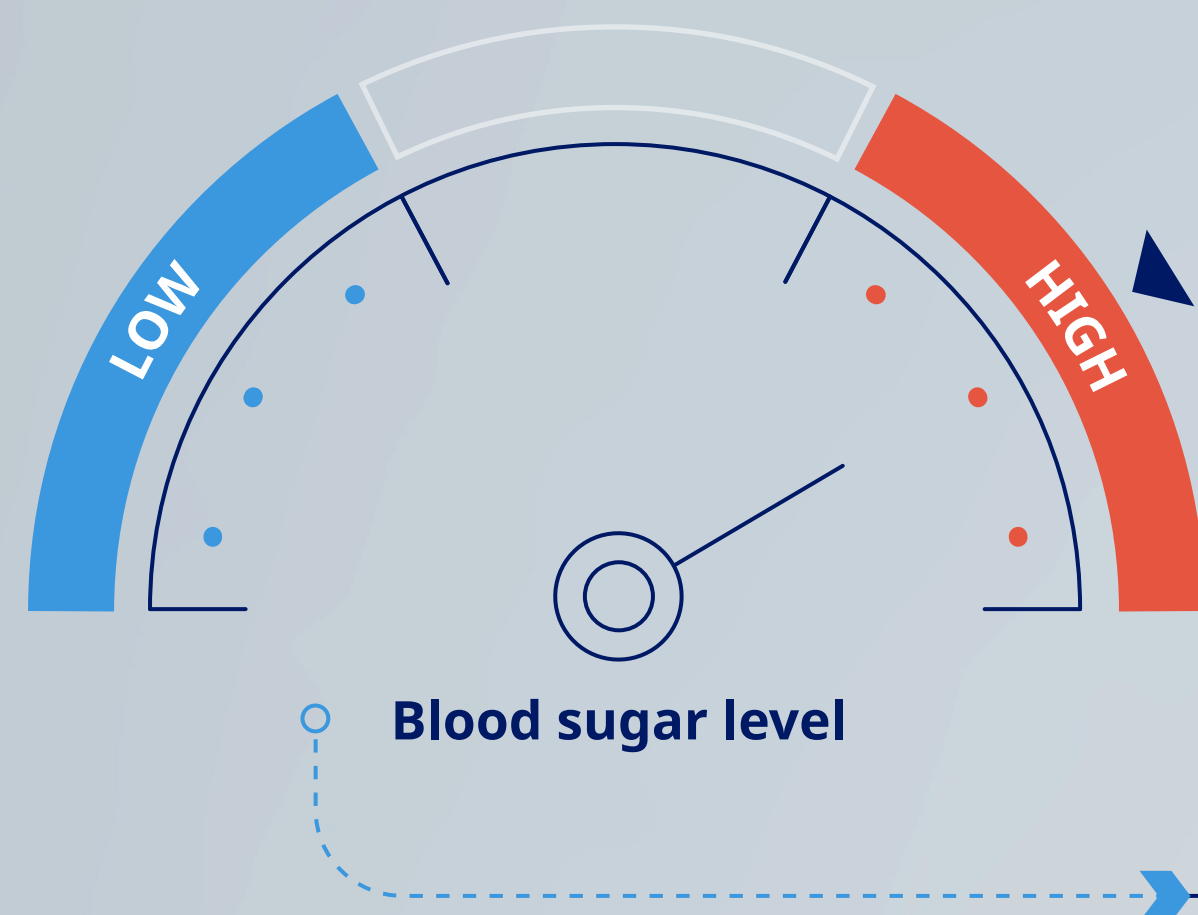
Please click either 'low' or 'high' on the dial to see how glucose levels affect the body



[BACK](#)

The importance of regulating postprandial hyperglycemia

Please click either 'low' or 'high' on the dial to see how glucose levels affect the body



After food intake, blood glucose levels rise resulting in the co-secretion of amylin and insulin¹

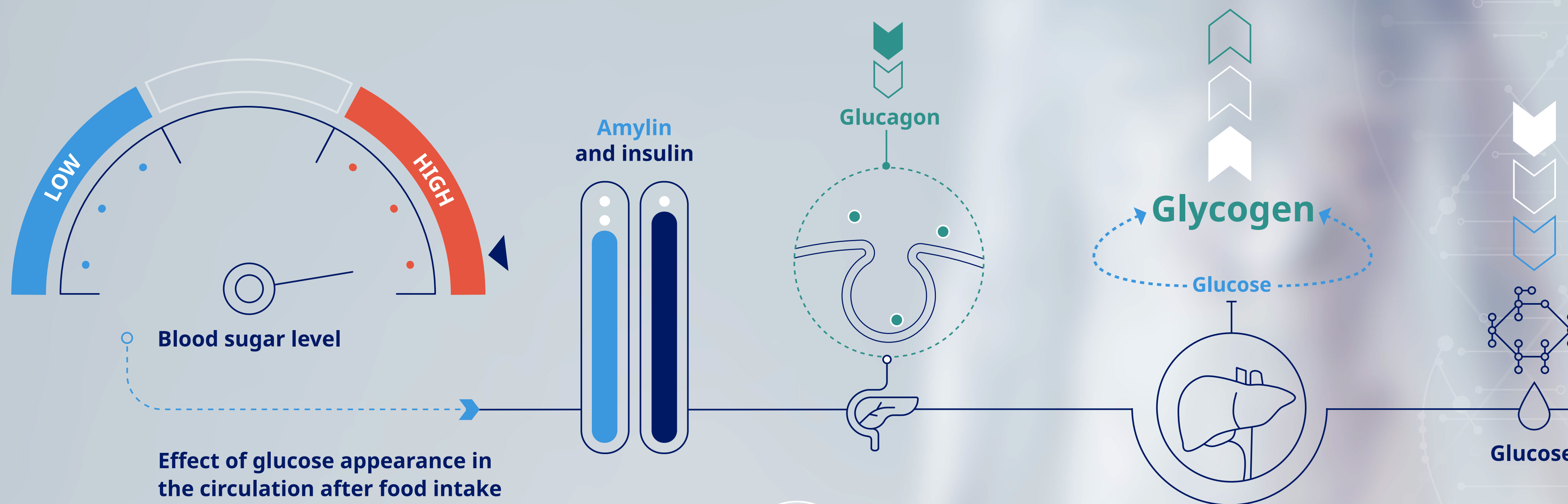
Insulin stimulates glucose uptake in tissues and inhibits glucose production in the liver, leading to lowered blood glucose levels¹

Amylin supports insulin by preventing rapid spikes in postprandial blood glucose levels,¹ through multiple mechanisms that we will explore throughout this module

[NEXT](#)

The importance of regulating postprandial hyperglycemia

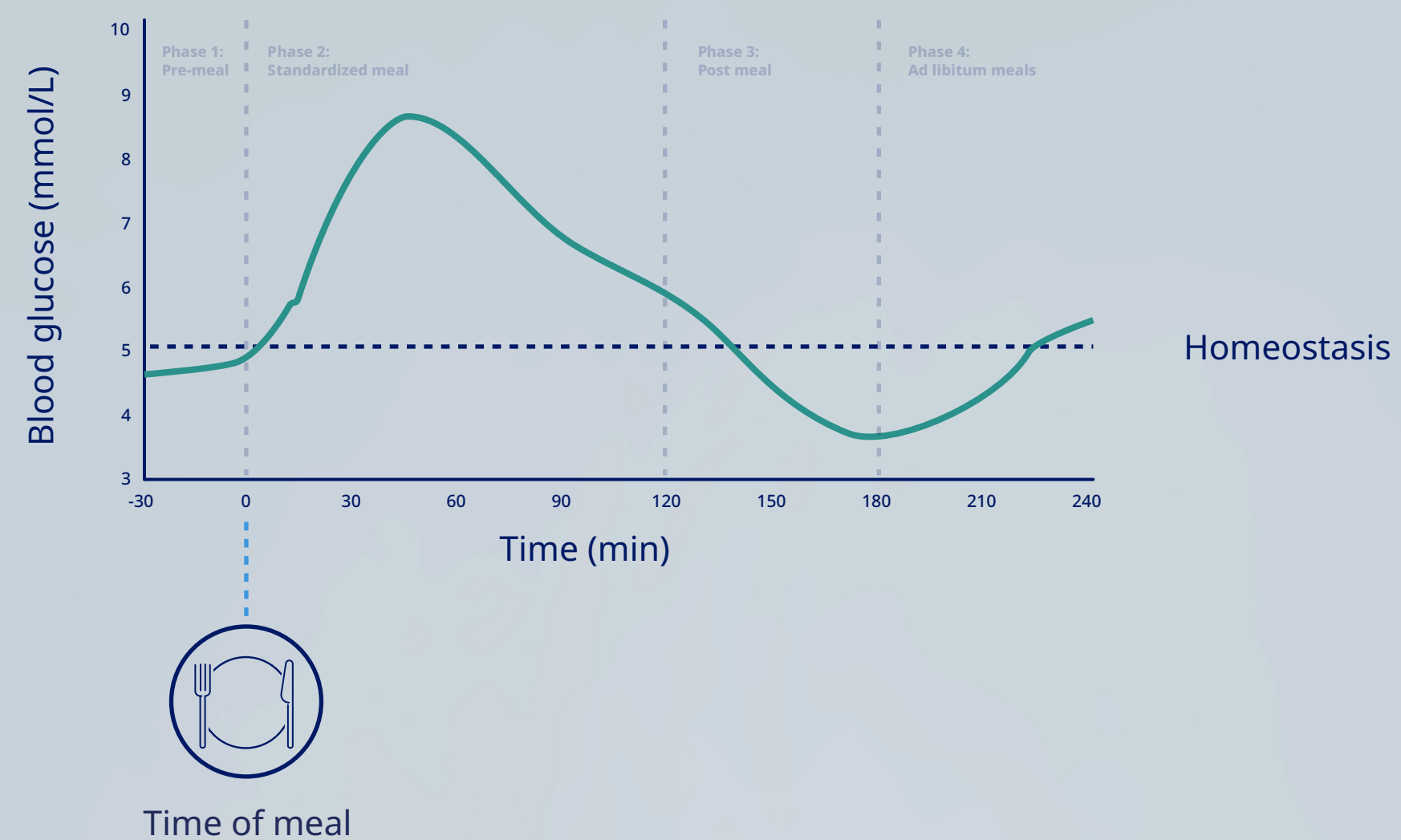
Please click either 'low' or 'high' on the dial to see how glucose levels affect the body



What role does amylin play in glucose metabolism?

Amylin is a key player in maintaining glucose homeostasis¹⁻⁴

Blood glucose levels during and after a meal in humans⁵



Amylin helps to lower postprandial blood glucose levels, contributing to maintained glucose homeostasis after meals¹

BACK

How does amylin regulate postprandial blood glucose levels?

Amylin achieves this through three main functions:^{2,3,6}



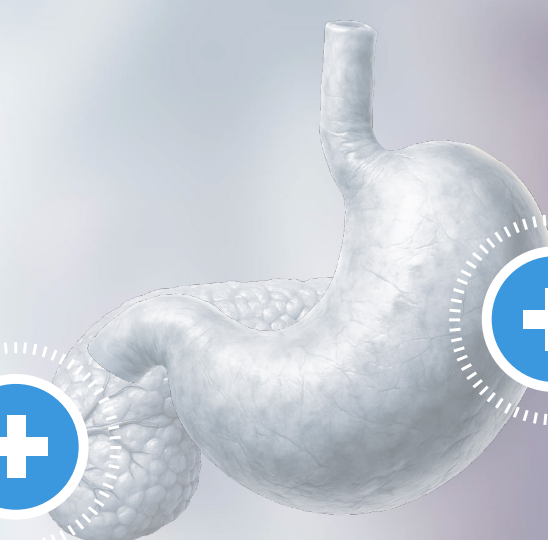
BRAIN



PANCREAS



GASTROINTESTINAL



NEXT

REFERENCES

How does amylin regulate postprandial blood glucose levels?

Amylin achieves this through three main functions:^{2,3,6}

BACK



BRAIN

Reducing food intake

PANCREAS



GASTROINTESTINAL

NEXT

REFERENCES

BACK

How does amylin regulate postprandial blood glucose levels?

Amylin achieves this through three main functions:^{2,3,6}



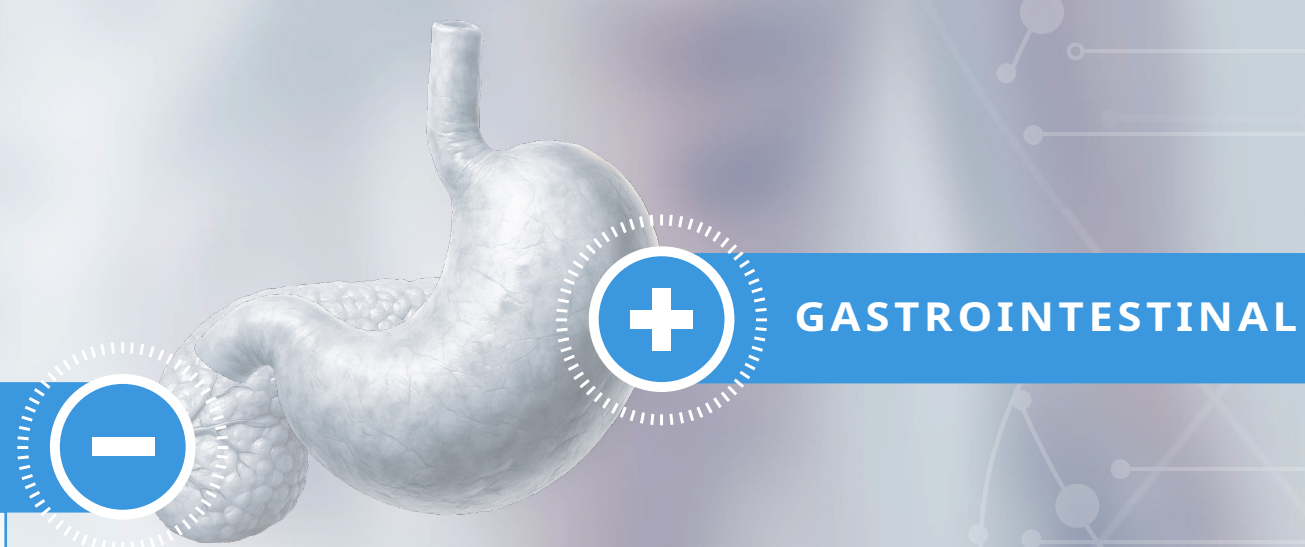
PANCREAS



Suppressing glucagon secretion



GASTROINTESTINAL



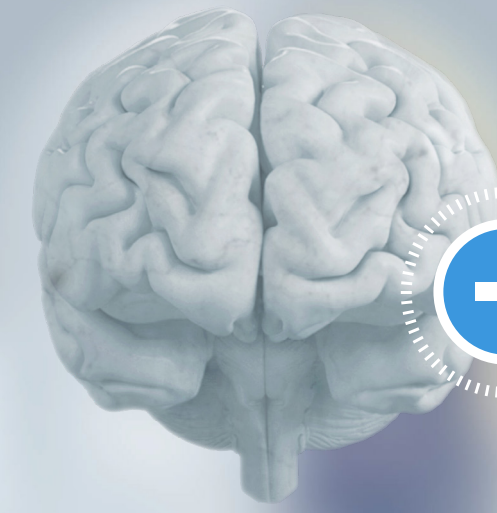
NEXT

REFERENCES

BACK

How does amylin regulate postprandial blood glucose levels?

Amylin achieves this through three main functions:^{2,3,6}



BRAIN

PANCREAS



GASTROINTESTINAL

Slowing the rate of gastric emptying

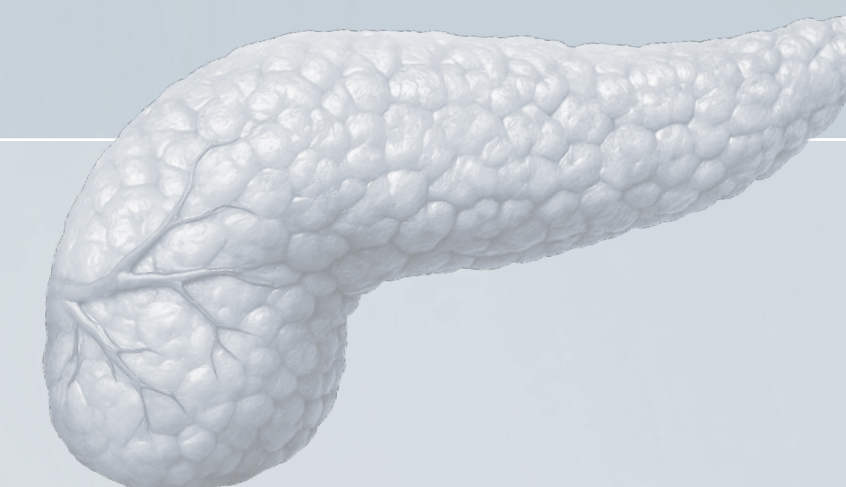
NEXT

REFERENCES

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How does amylin regulate postprandial blood glucose levels?

Amylin is a nutrient-stimulated hormone that is co-secreted with insulin from pancreatic β cells in response to food intake^{3,7}

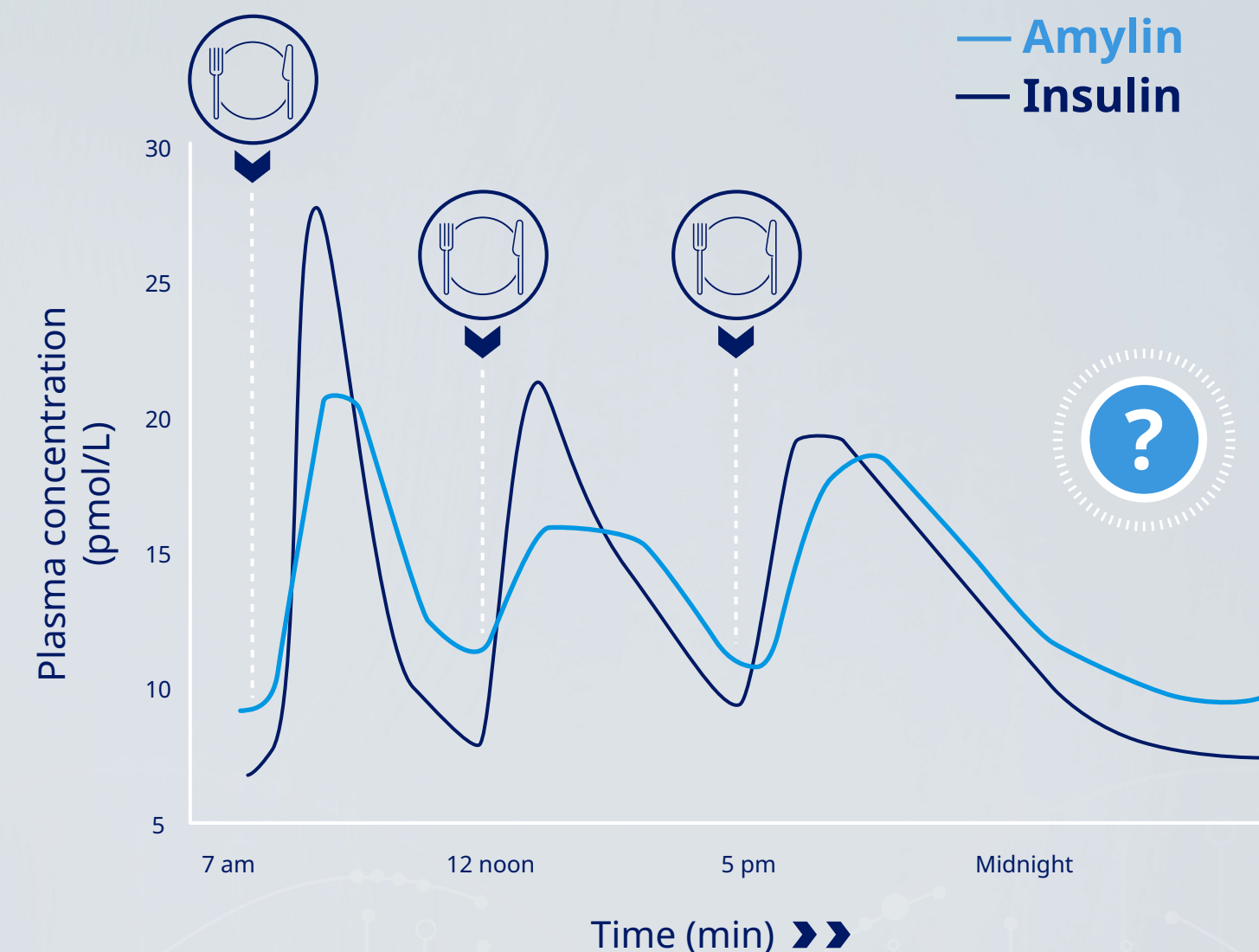
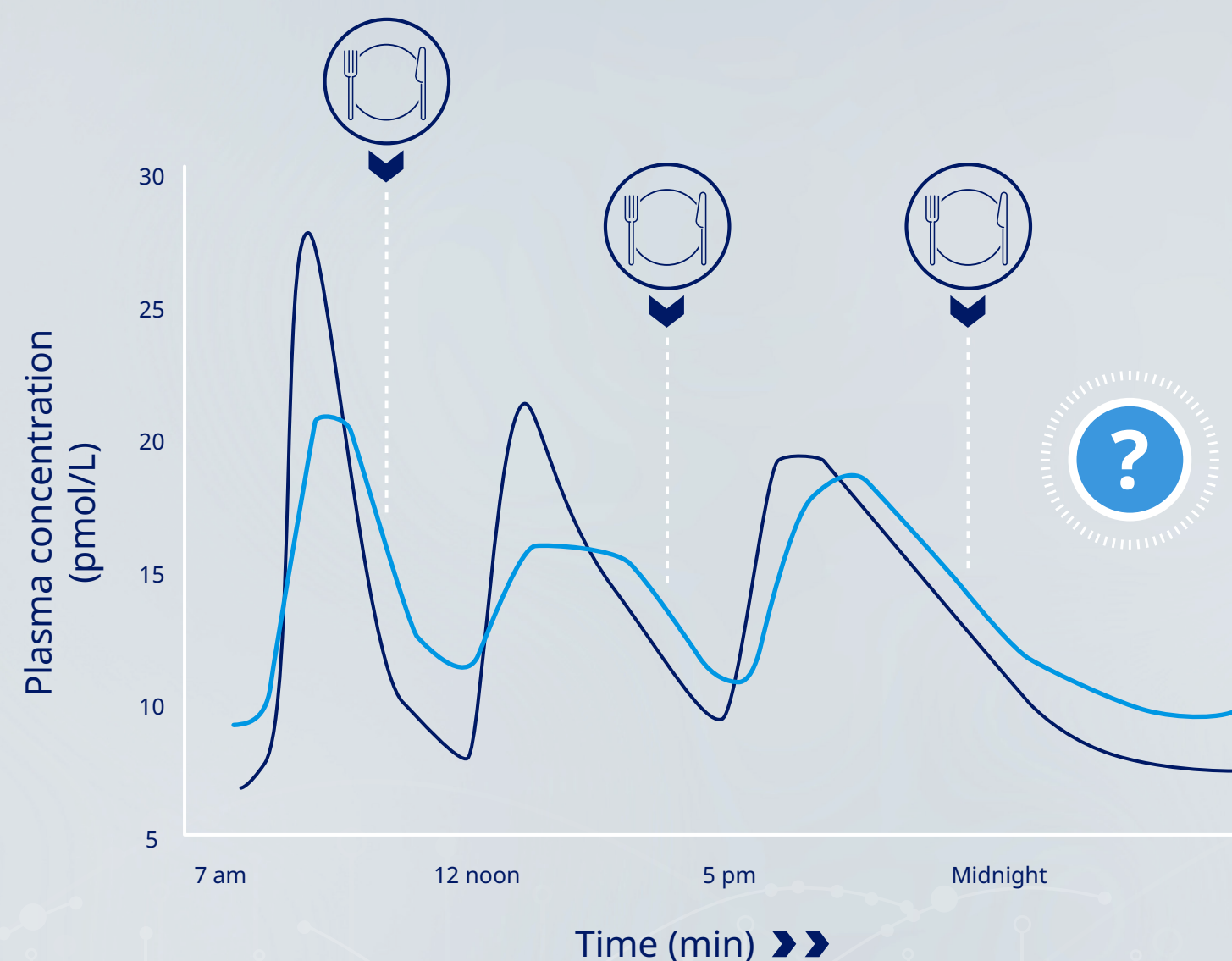


PANCREAS

How does amylin regulate postprandial blood glucose levels?

Here are two graphs showing plasma amylin and insulin concentrations in healthy individuals (n=6), with plates indicating mealtimes¹

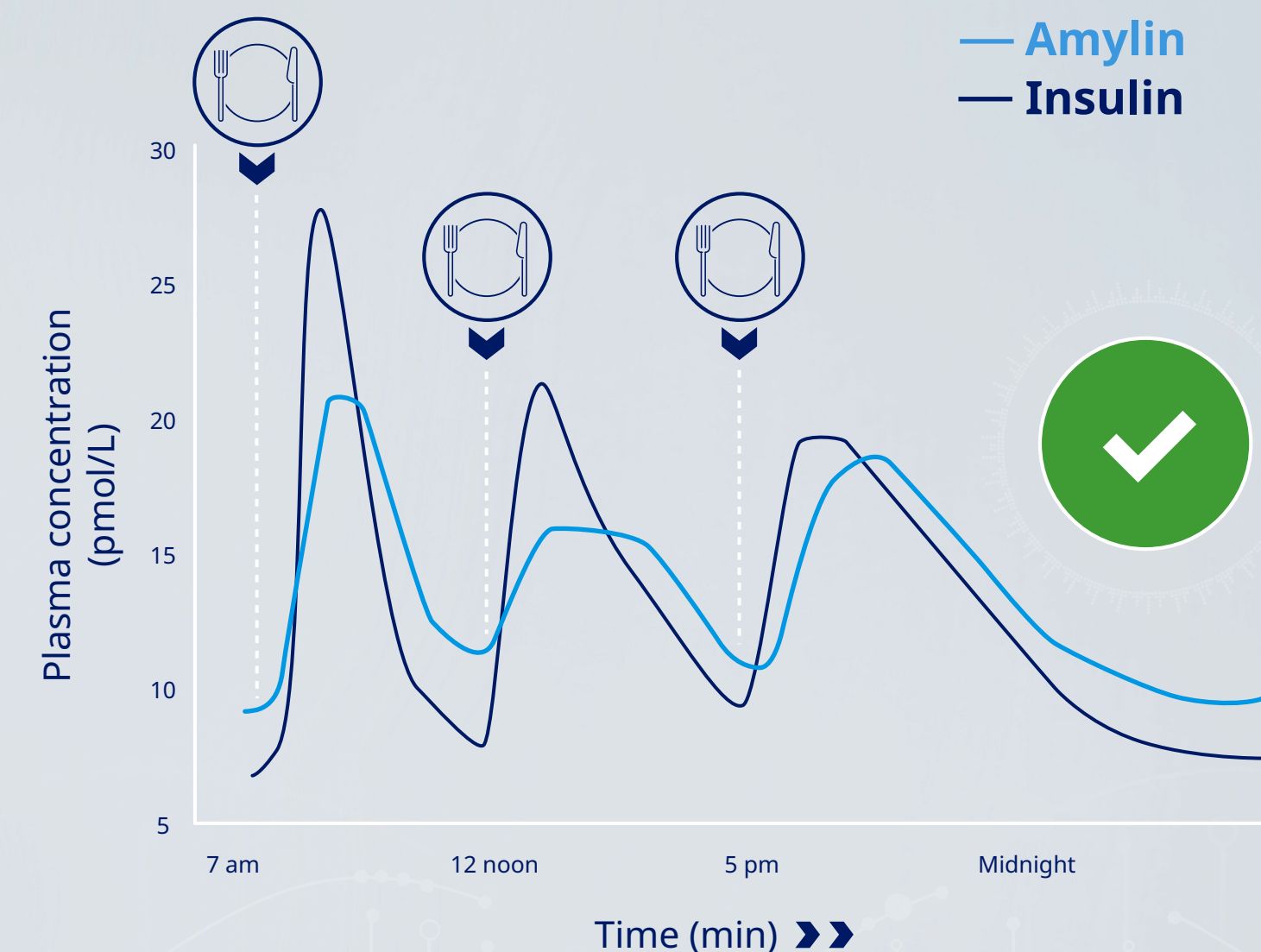
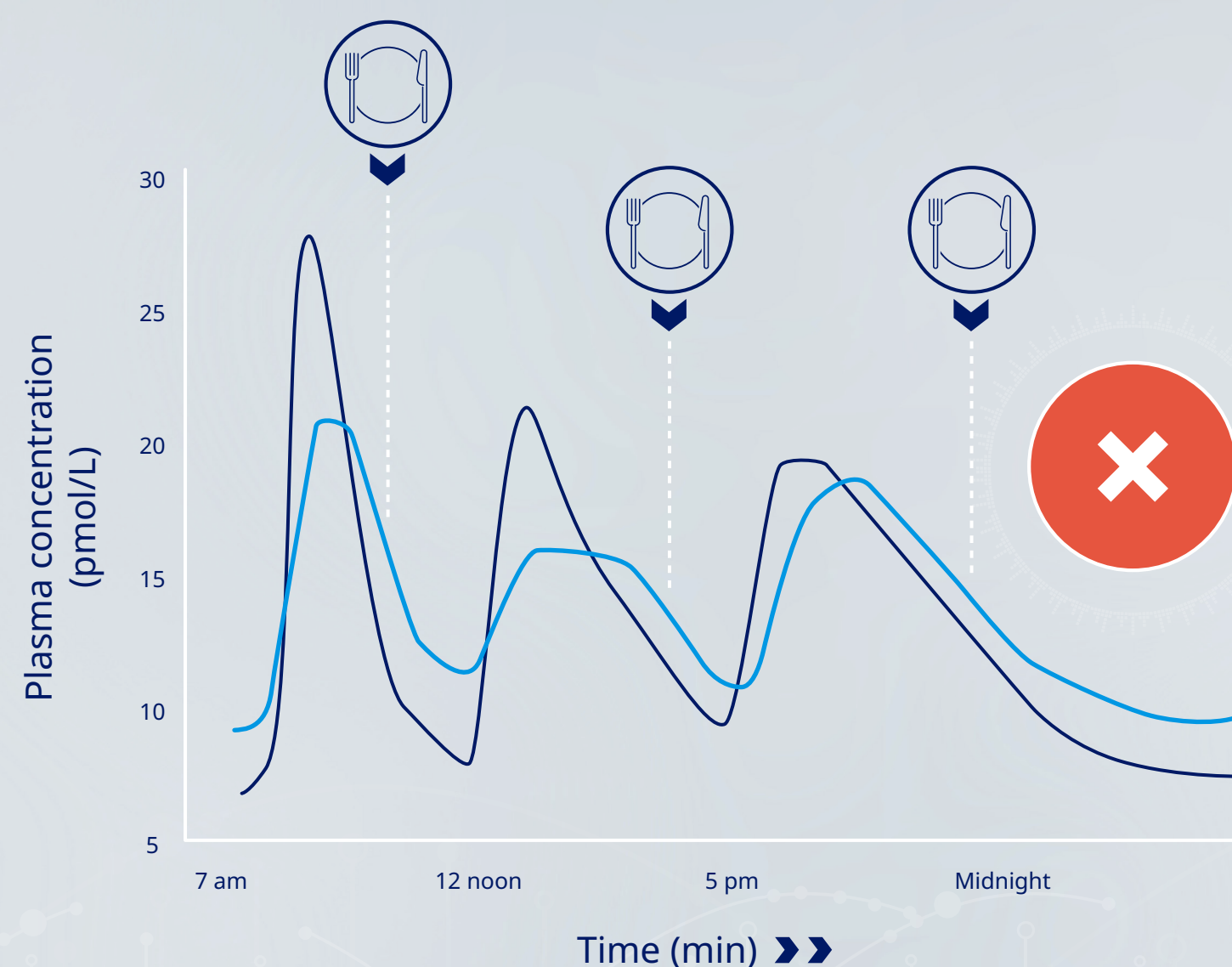
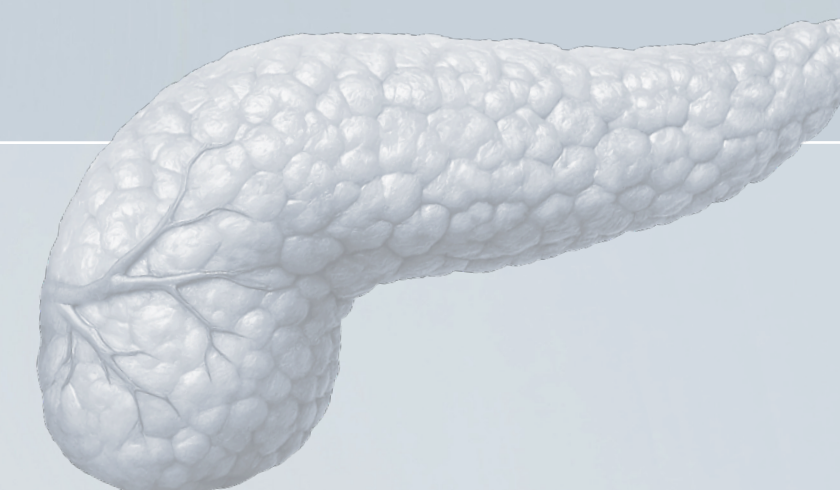
Click which figure you think correctly represents amylin and insulin concentrations after a meal



PANCREAS

How does amylin regulate postprandial blood glucose levels?

The graph on the right is correct. Following a meal, there is a sharp postprandial increase in plasma concentrations of both insulin and amylin¹

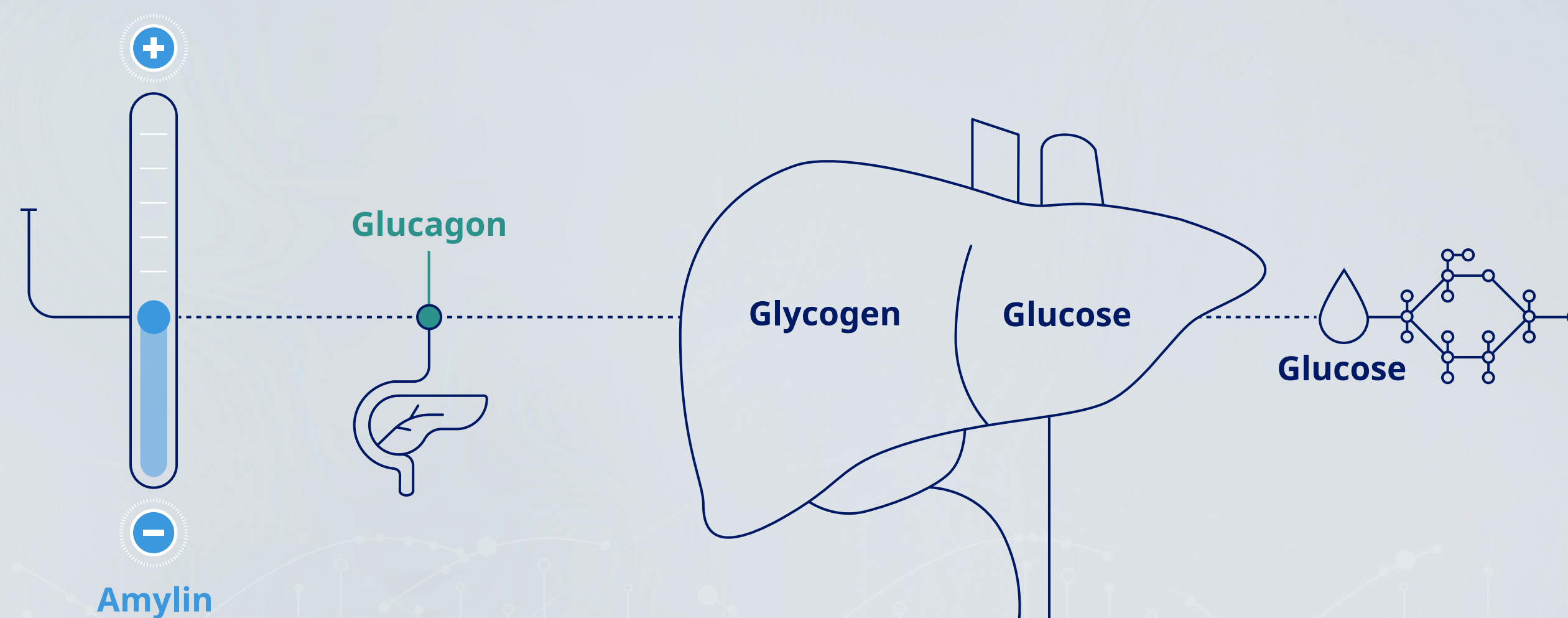


PANCREAS

How does amylin regulate postprandial blood glucose levels?

Glucagon stimulates glucose production in the liver^{1,2,6}

Please click the + and – buttons to see how increased or decreased amylin levels impact glucagon production



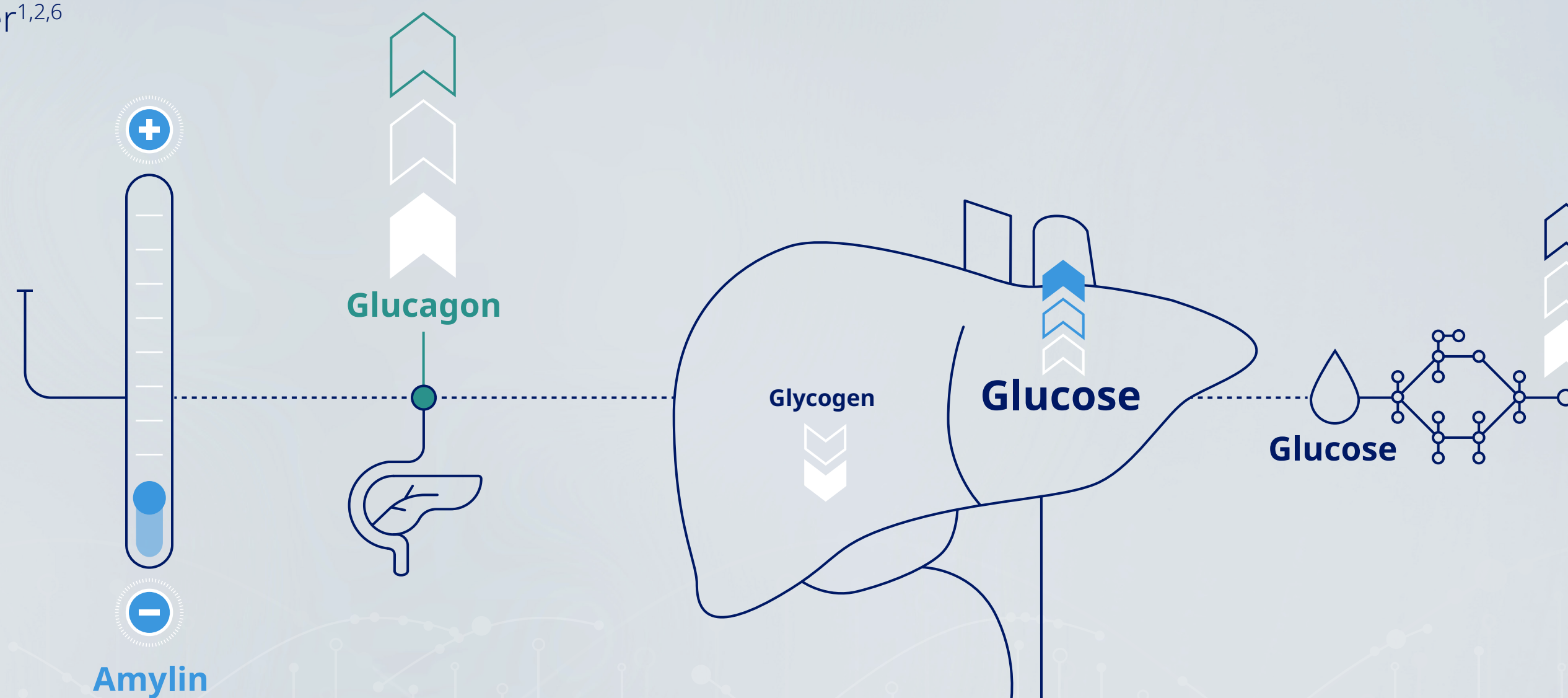
PANCREAS

How does amylin regulate postprandial blood glucose levels?

Glucagon stimulates glucose production in the liver^{1,2,6}

Low concentrations of amylin lead to increased concentrations of glucagon secreted from the α cells of the pancreas. This results in increased levels of glucose available for absorption^{1,2}

Please click the + and – buttons to see how increased or decreased amylin levels impact glucagon production



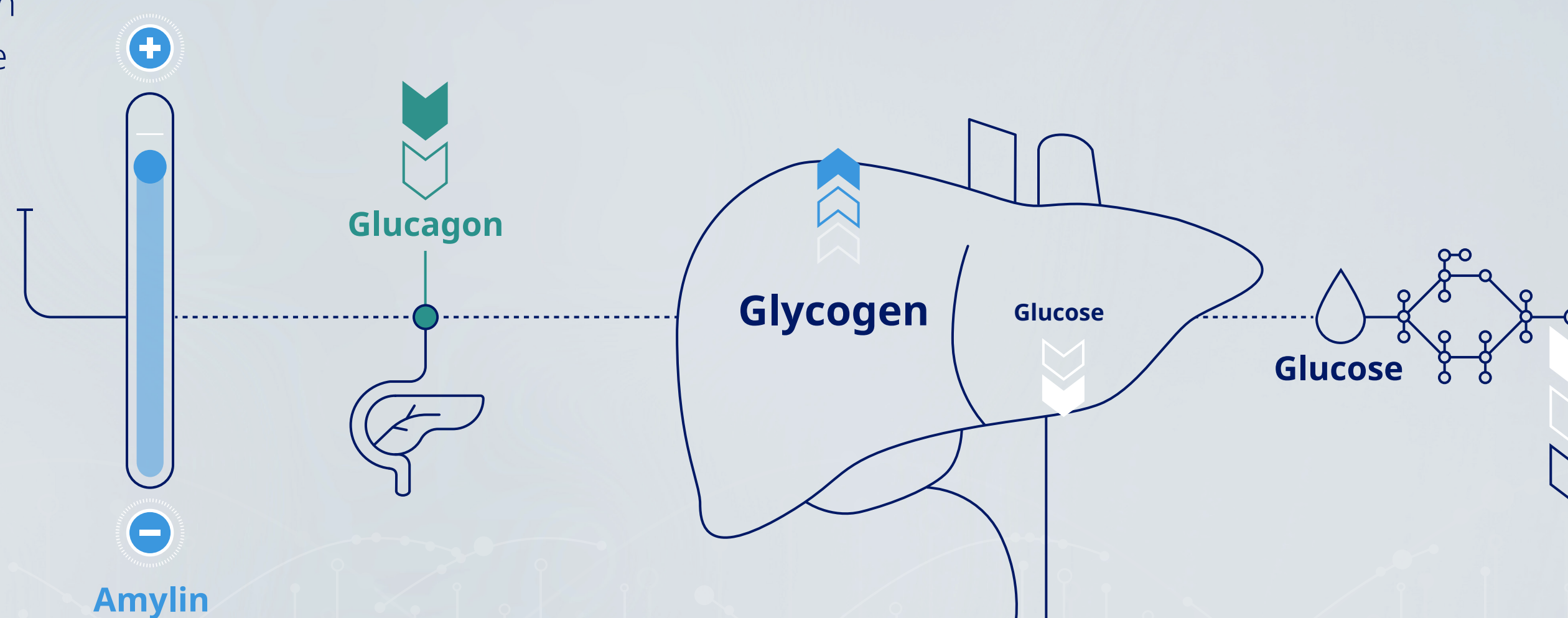
PANCREAS

How does amylin regulate postprandial blood glucose levels?

Glucagon stimulates glucose production in the liver^{1,2,6}

Amylin suppresses the postprandial α -cell secretion of glucagon, thereby reducing the post-meal surge in glucose levels^{1,2,6}

Please click the + and – buttons to see how increased or decreased amylin levels impact glucagon production



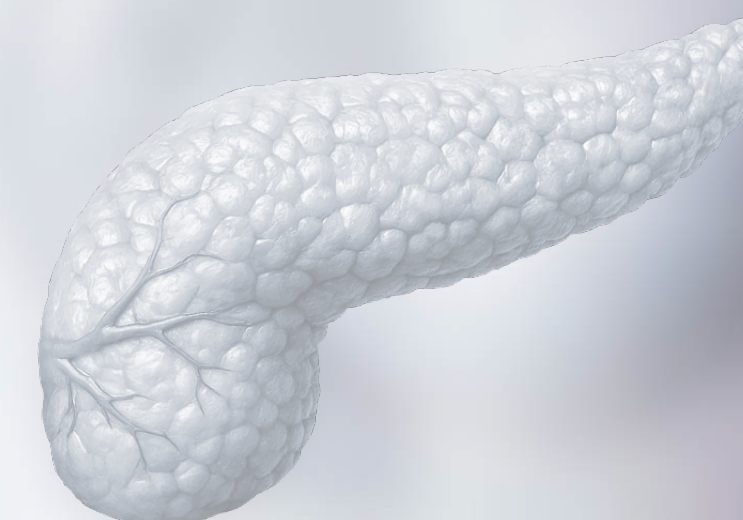
BACK

PANCREAS

How does amylin regulate postprandial blood glucose levels?

Following food intake in people without diabetes, insulin and amylin are co-secreted into the circulation leading to a sharp and robust postprandial increase in the plasma concentration of both hormones¹

Data from rodent studies have shown that amylin complements the effects of insulin in postprandial glucose homeostasis by two independent mechanisms, gastric emptying and by helping to control glucagon secretion¹



NEXT

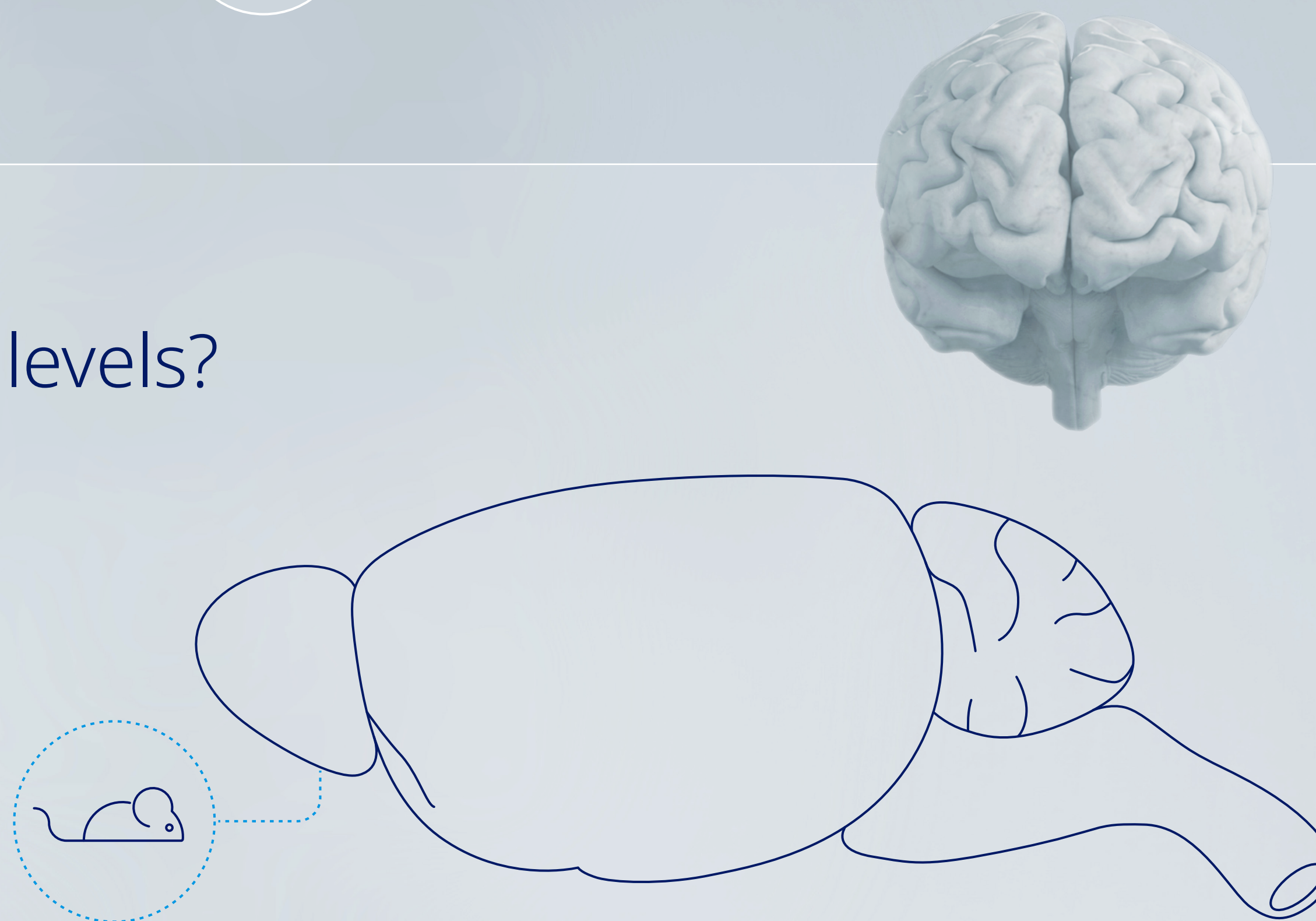
REFERENCES

BRAIN

How does amylin regulate postprandial blood glucose levels?

Data from rodents have demonstrated that amylin mediates its effects via the central nervous system^{3,6,8}

Explore the regions of the central nervous system involved in mediating the effects of amylin



PRIMARY SITE
OF ACTIVATION



OTHER SITES
OF ACTIVATION

BRAIN

How does amylin regulate postprandial blood glucose levels?

Extensive studies in primates and rodents have identified the primary sites of amylin activation¹

The highest affinity of amylin binding sites has been found in the area postrema of the brainstem, where approximately 90% of neurons that sense glucose also express amylin receptors¹

Numerous studies have demonstrated that amylin binding in the area postrema of the brainstem propagates signals to the nucleus of the solitary tract and lateral parabrachial nucleus^{3,6,8}



PRIMARY SITE
OF ACTIVATION



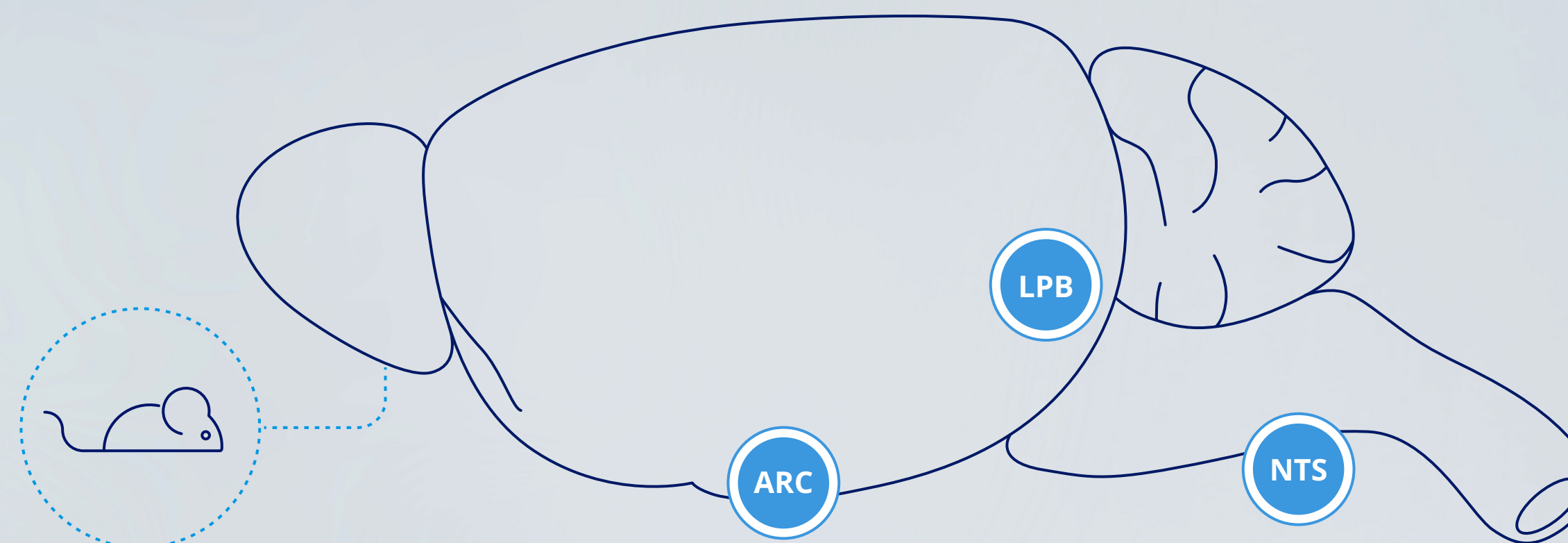
OTHER SITES
OF ACTIVATION

AP, area postrema; LPB, lateral parabrachial nucleus; NTS, nucleus of the solitary tract.

BRAIN

How does amylin regulate postprandial blood glucose levels?

Rodent data have shown that other sites in the central nervous system that mediate amylin action include the nucleus of the solitary tract and lateral parabrachial nucleus, which convey signals to the hypothalamus^{3,6}

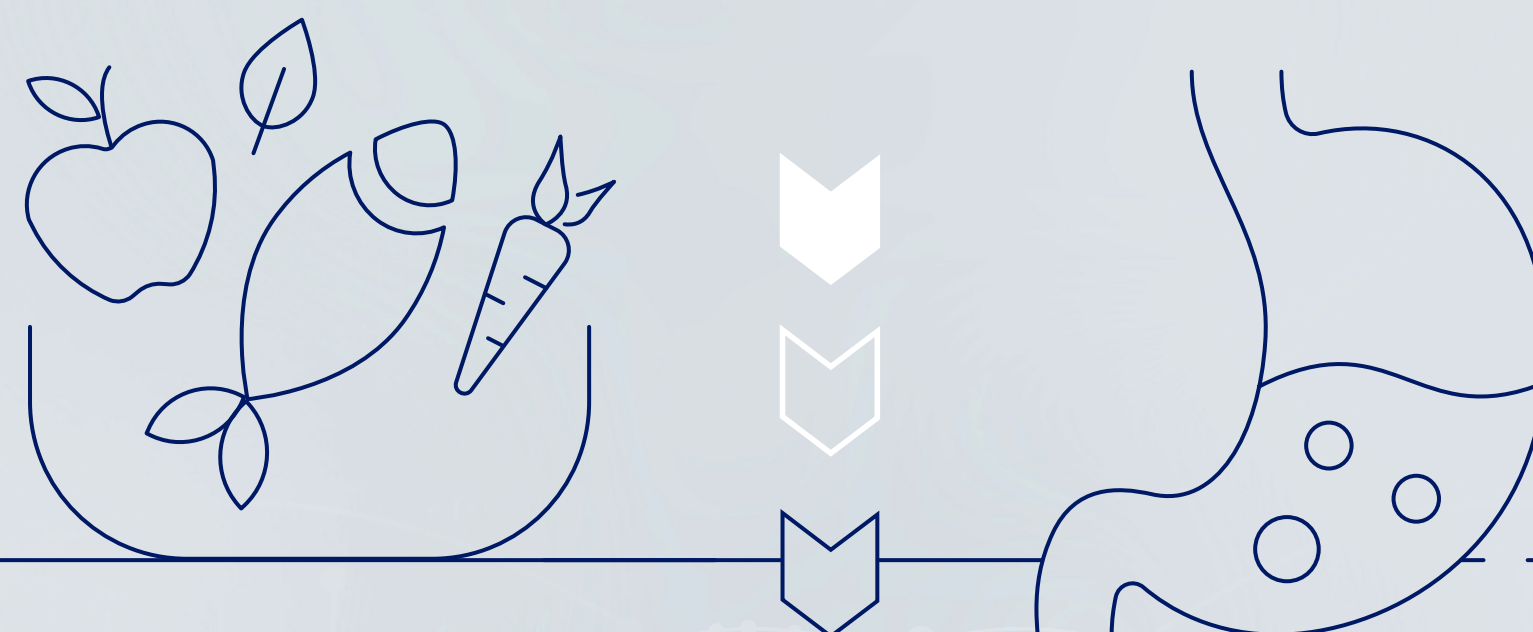


ARC, arcuate nucleus; LPB, lateral parabrachial nucleus; NTS, nucleus of the solitary tract.

BRAIN

How does amylin regulate postprandial blood glucose levels?

Binding of amylin to neurons in these brain regions regulates appetite by promoting feelings of fullness and reducing food intake. This leads to a reduced amount of digested food available from which glucose can be absorbed^{3,6,8}



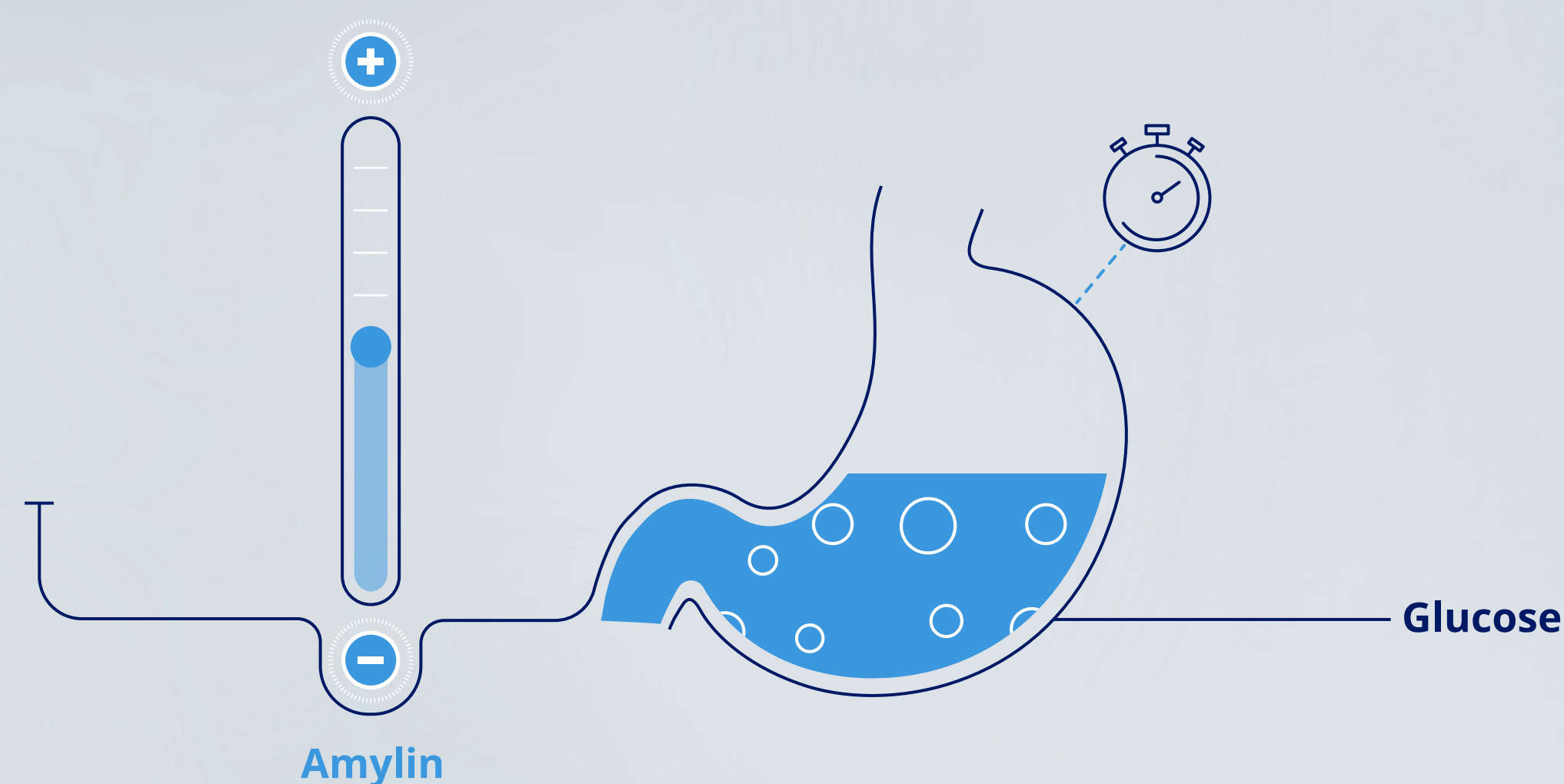
[BACK](#)

GASTROINTESTINAL

How does amylin regulate postprandial blood glucose levels?

Amylin reduces the amount of glucose available for absorption by regulating gastric emptying^{3,6}

Please click the + and – buttons to see how increased or decreased amylin levels impact gastric emptying


[NEXT](#)
[REFERENCES](#)

[BACK](#)

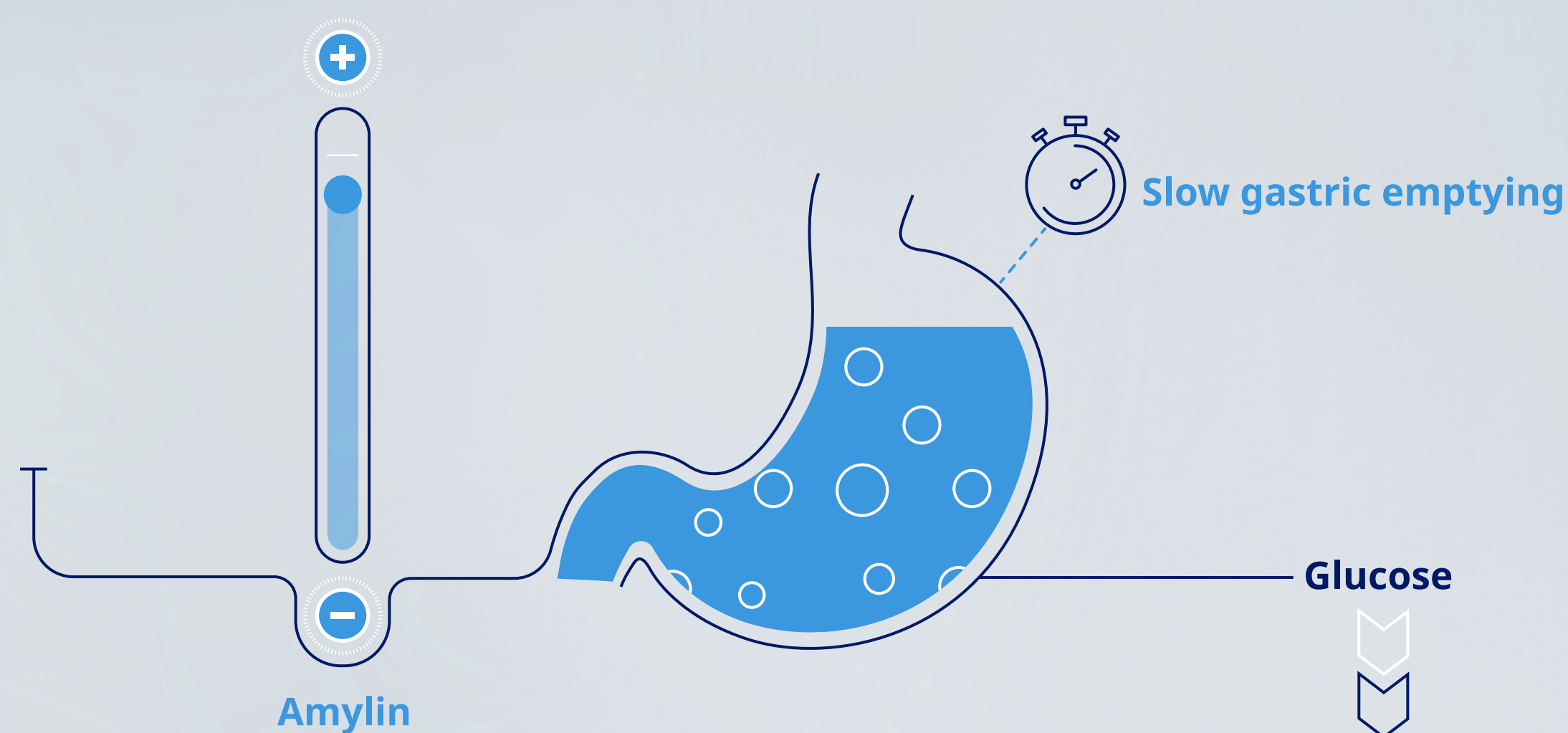
GASTROINTESTINAL

How does amylin regulate postprandial blood glucose levels?

In addition to regulating appetite, amylin also reduces the rate of gastric emptying^{3,6}

High concentrations of amylin slows the rate of gastric emptying, reducing the amount of glucose available for absorption, helping to lower blood glucose levels after a meal. This action is mediated by the area postrema and efferent vagal nerves^{1,3,6}

Please click the + and – buttons to see how increased or decreased amylin levels impact gastric emptying


[NEXT](#)
[REFERENCES](#)

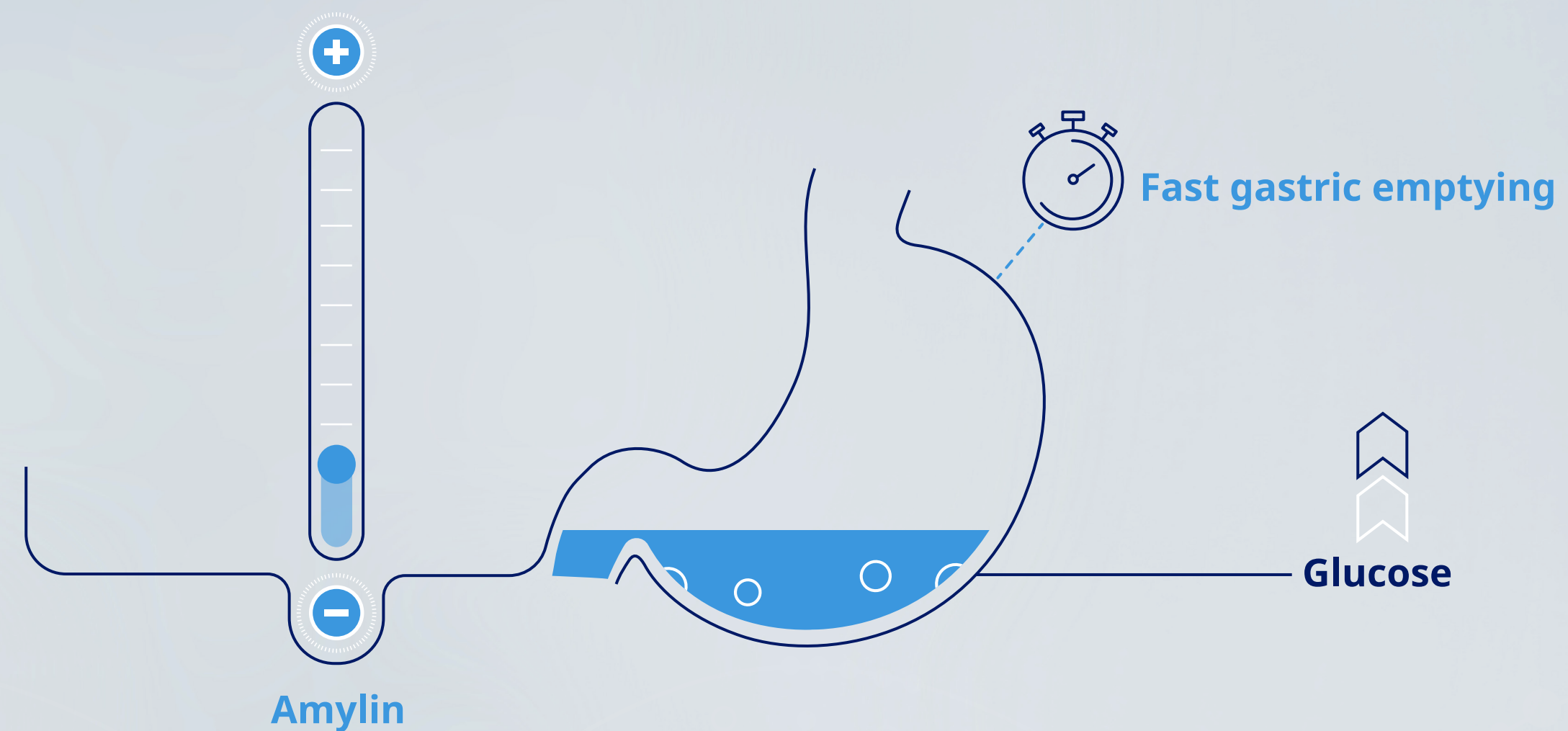
GASTROINTESTINAL

How does amylin regulate postprandial blood glucose levels?

In addition to regulating appetite, amylin also reduces the rate of gastric emptying^{3,6}

When amylin concentrations are low, the rate of gastric emptying increases, resulting in more glucose becoming available for absorption^{1,3,6}

Please click the + and – buttons to see how increased or decreased amylin levels impact gastric emptying

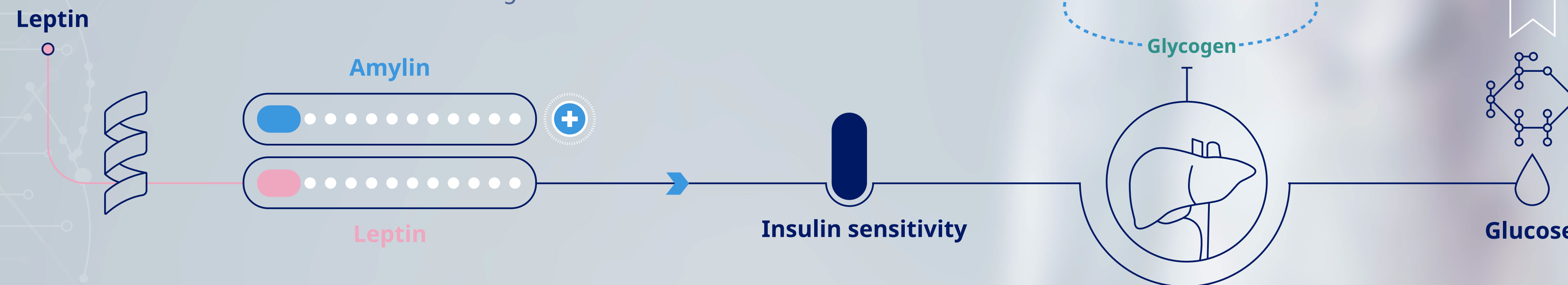


How does amylin work with leptin to manage blood glucose levels?

Amylin can mediate the effects of other nutrient-stimulated hormones to have synergistic effects on eating^{3,9}

Animal studies have shown that leptin can increase insulin sensitivity by enhancing insulin-mediated glucose uptake into tissues and inhibition of liver glucose production^{9,10}

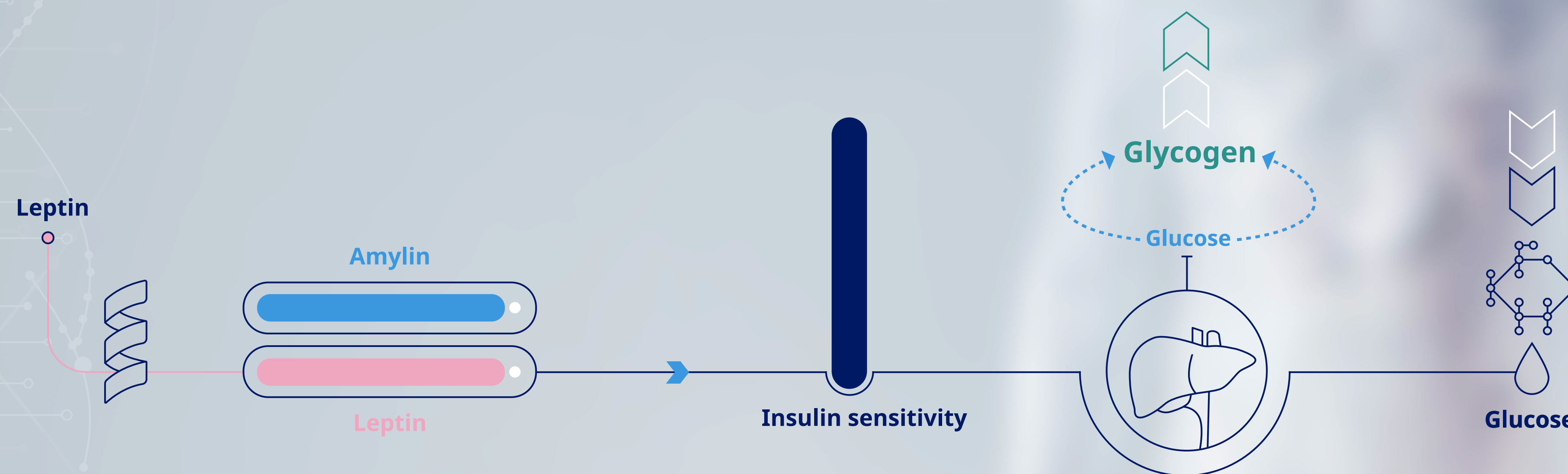
Please click the + button to see how increased amylin levels impact leptin concentration and blood glucose



How does amylin work with leptin to manage blood glucose levels?

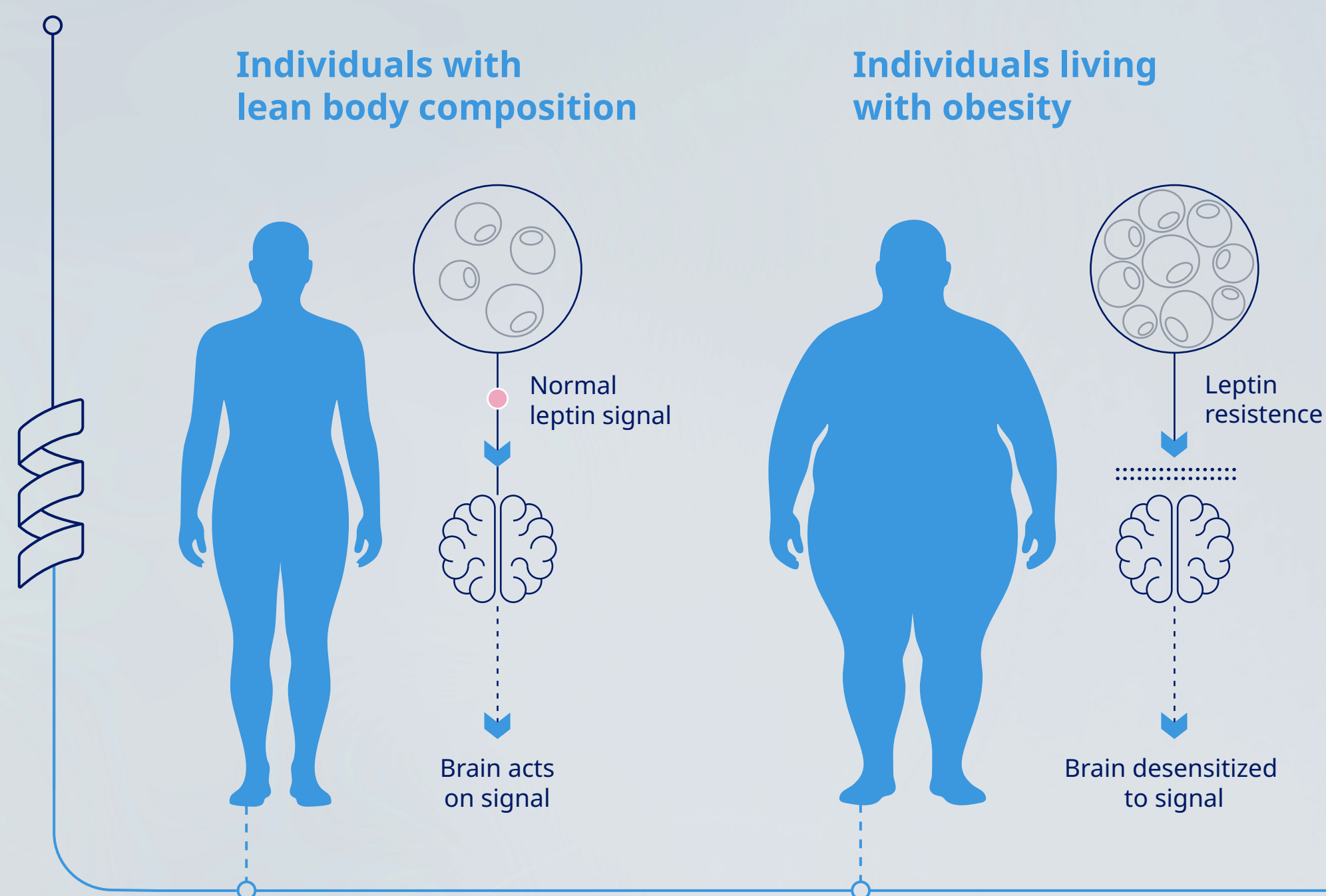
Leptin can increase insulin sensitivity by enhancing insulin-mediated glucose uptake into tissues and inhibition of liver glucose production^{9,10}

In rodent studies, amylin has been shown to have a synergistic effect on leptin signaling via enhancing leptin binding in the central nervous system¹¹



How does amylin affect leptin resistance?

In people living with obesity, despite having high circulating leptin levels, there is resistance to leptin⁹



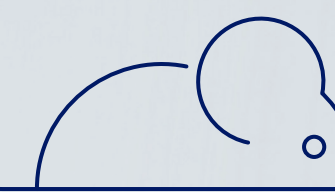
BACK

How does amylin work with other hormones to manage blood glucose levels?

Click the + button to see the effects of co-administrated leptin and amylin on leptin-resistant mice



**Leptin
and amylin**



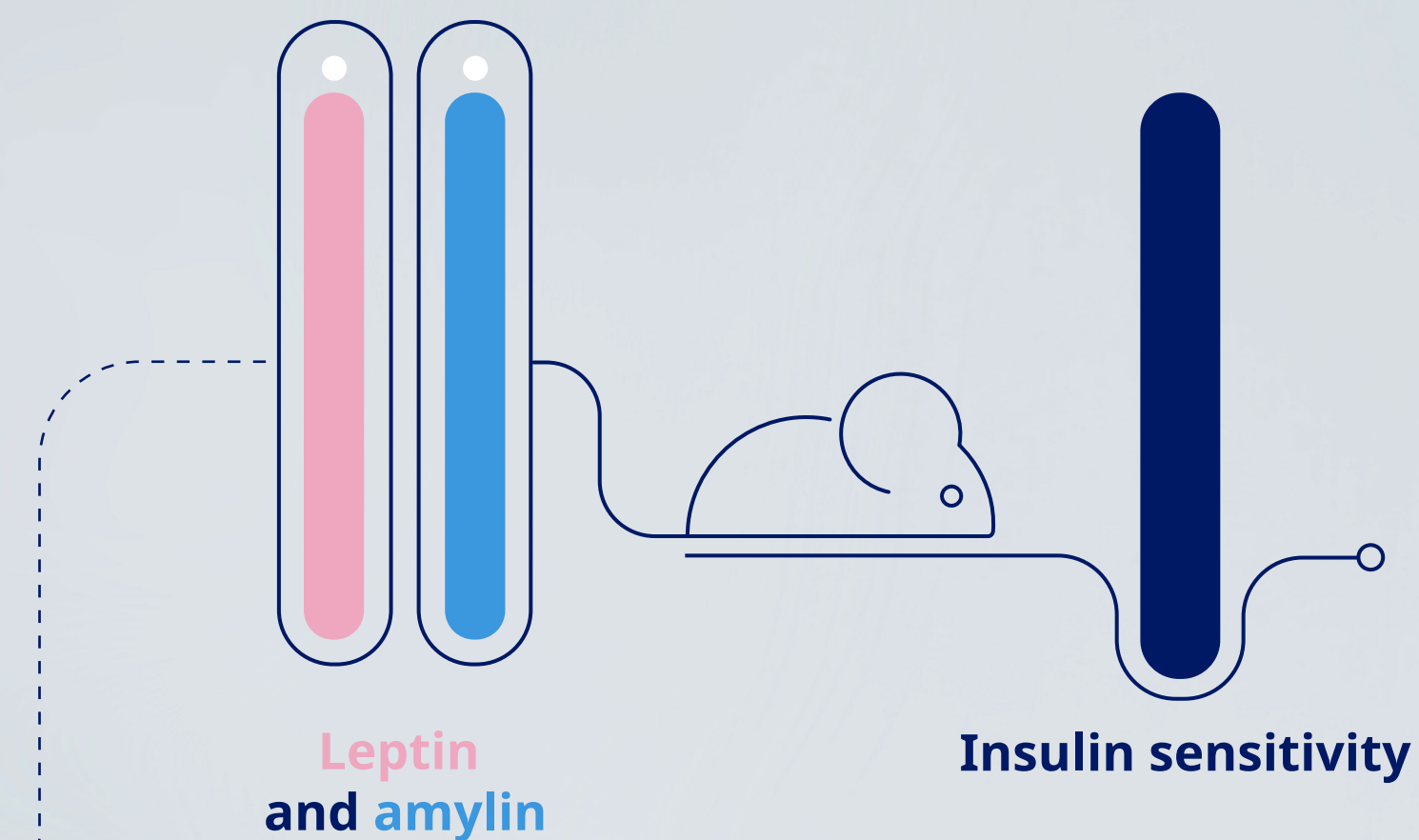
Insulin sensitivity

NEXT

REFERENCES

How does amylin work with other hormones to manage blood glucose levels?

Animal studies have demonstrated that co-administration of leptin and amylin enhanced insulin sensitivity in leptin-resistant diet-induced obese mice, compared with leptin or amylin alone⁹



Do amylin levels differ in people living with diabetes?

In people living with diabetes, amylin function is often compromised¹

Please click on each patient group to see how amylin activity may vary

-  **People living without T1D/T2D**
-  **People living with T1D**
-  **People living with T2D using insulin**



Do amylin levels differ in people living with diabetes?

In people living with diabetes, amylin function is often compromised¹

Please click on each patient group to see how amylin activity may vary



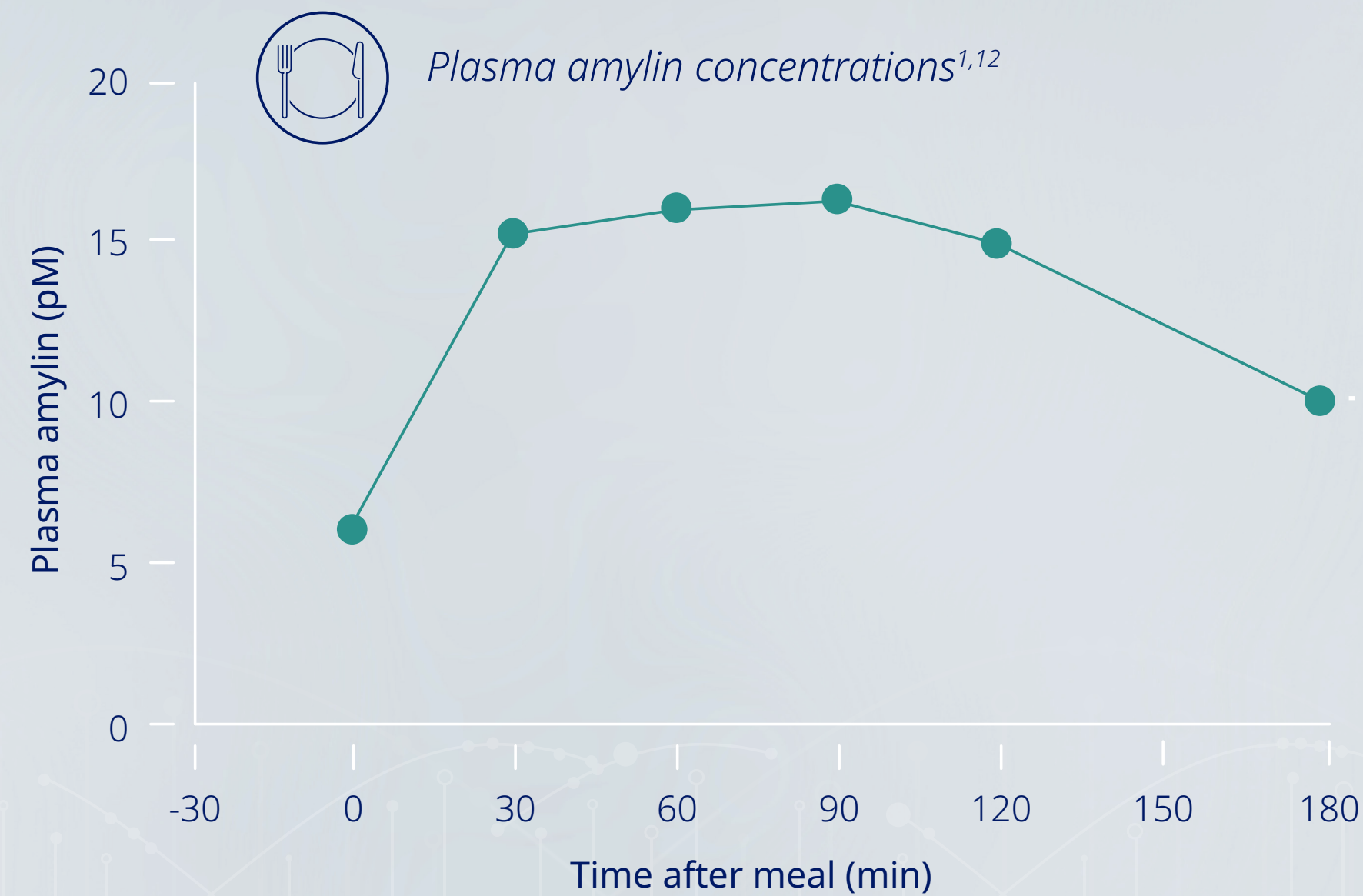
People living without T1D/T2D



People living with T1D



People living with T2D using insulin



In people without diabetes, there is a sharp increase in plasma amylin concentrations following a meal¹

Do amylin levels differ in people living with diabetes?

In people living with diabetes, amylin function is often compromised¹

Please click on each patient group to see how amylin activity may vary



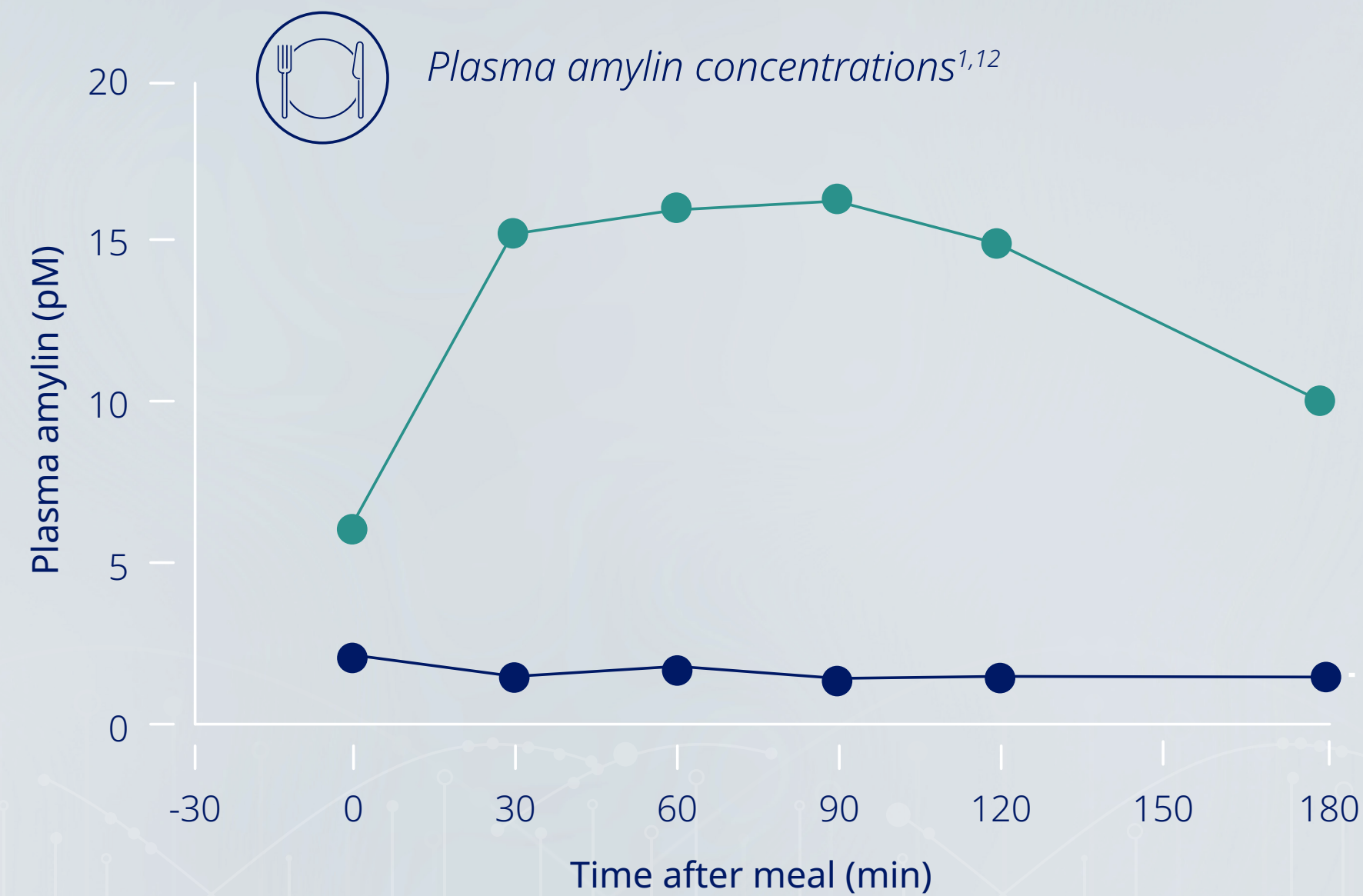
People living without T1D/T2D



People living with T1D



People living with T2D using insulin



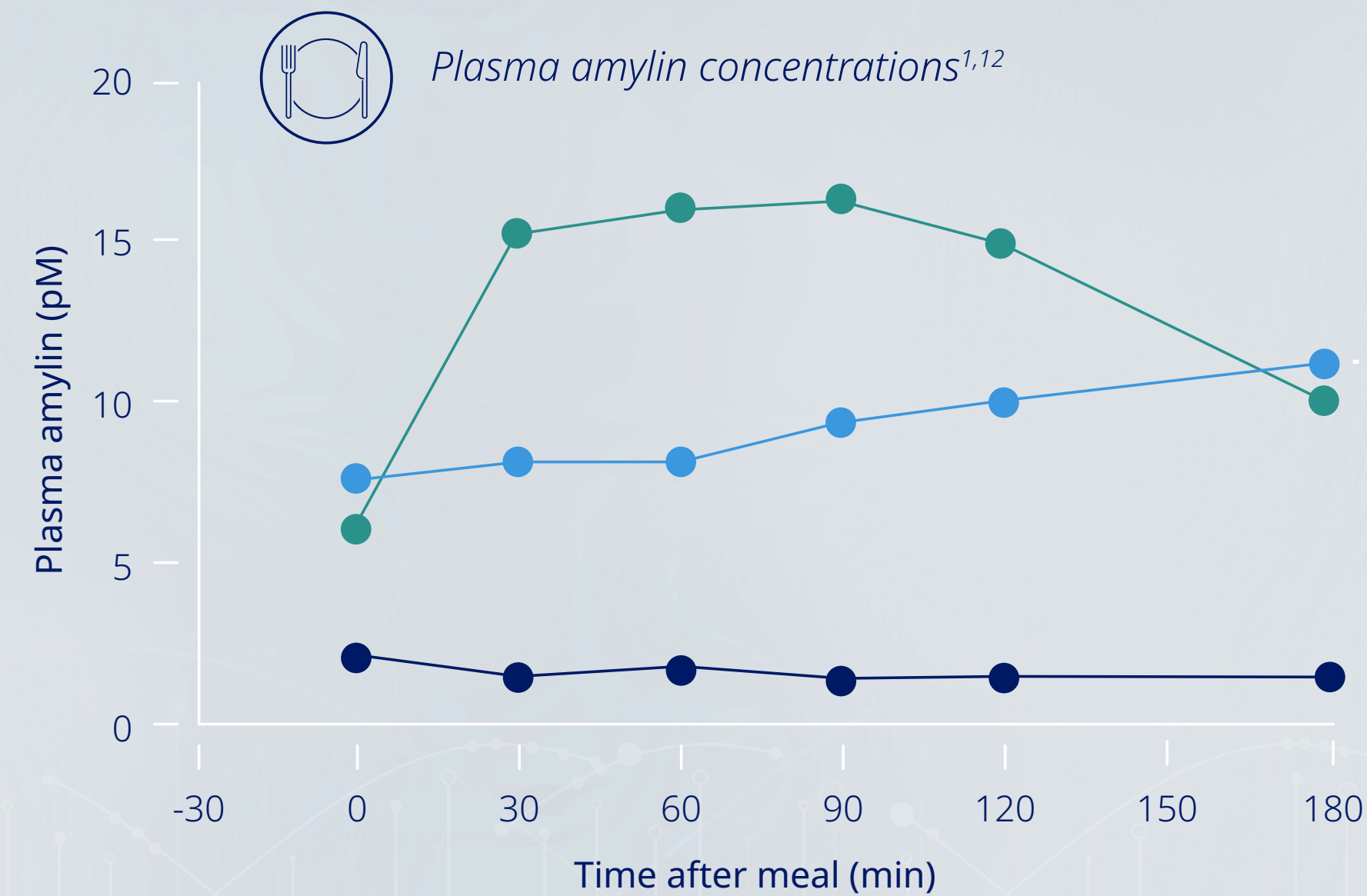
People living with T1D have an absolute deficiency of amylin and insulin^{1,12}

Do amylin levels differ in people living with diabetes?

In people living with diabetes, amylin function is often compromised¹

Please click on each patient group to see how amylin activity may vary

- 1  **People living without T1D/T2D**
- 2  **People living with T1D**
- 3  **People living with T2D using insulin**



People living with T2D have a relative deficiency of amylin and insulin, along with an impaired response of these hormones to food intake^{1,12}

Summary

In summary, amylin plays a crucial role in glucose metabolism by **reducing food intake, slowing the rate of gastric emptying and suppressing glucagon secretion**^{2,3,6}

These mechanisms help maintain stable postprandial blood glucose levels. By interacting with other hormones, amylin contributes to a complex network that regulates glucose homeostasis, underscoring its important role in overall metabolism¹



BRAIN

Reducing food intake



PANCREAS

GASTROINTESTINAL

Slowing the rate of gastric emptying

Suppressing glucagon secretion



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