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IN THIS EDITION

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Editors' Note

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This edition would not have been possible without the hard work of our dedicated editorial team. We would also like to thank Mr. Reeves and Dr. Griffin for their guidance and support for running the journal.

We're delighted to share the Trinity 2025 edition of the LGS Young Scientists' Journal, continuing to spark curiosity and enthusiasm for STEM throughout our school. This vibrant platform enables students to investigate scientific concepts, present research, and take part in thoughtful dialogue, reflecting their commitment and passion.

This term, we feature engaging articles on the gut-brain axis, tea's calming effects, and quantum cryptography's double-edged potential. From faecal transplants turning waste into cure to the weight-loss race between fasting and Ozempic, our writers have tackled cutting-edge topics with insight and dedication. We hope this edition inspires curiosity—and invite more students to contribute in the next edition.

Cover Images:

'The inner structures of the brain' by K H Fung

'Man with joint pain' by PIXOLOGICSTUDIO

'Ozempic' by Eggy Sayoga

'Huntington's disease' by Drug Target Review

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TRINITY 2025

The Gut-Brain Axis: Linking Microbes and the Mind

Key Words:

Microbe: an extremely small living thing, such as a bacterium, that can only be seen with a microscope

Inflammation: a condition where a part of the body becomes red, painful, and swollen, often in response to infection or injury

By Abhiram Varanasi (Year 11)

The human gut is home to trillions of microbes, outnumbering our own cells, which can influence digestion, immunity, brain function. These microbes communicate with the brain through a vast network of nerves, hormones and immune signals in a system called the gut-brain axis. More information is transmitted between the gut and brain than any other system; the gut containing more nerve cells than anywhere else apart from the brain. This intimate connection suggests that disruptions in the gut microbiome can affect memory, mood and behaviour, meaning what we eat can influence how we feel.

What is the Gut-Brain Axis?

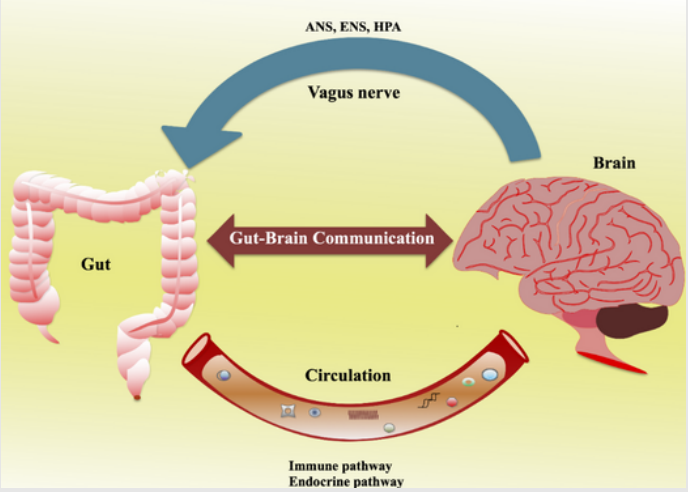

Figure 1. A graphic representation of the gut-brain axis (Suganya, 2020)

The gut-brain axis mainly operates through the enteric nervous system (ENS), which is a complex network of neurons embedded in the walls of the gastrointestinal tract - it's even called the "second brain" as it can operate somewhat independently from the central nervous system. The two systems are primarily connected via the vagus nerve, which carries sensory signals about satiety and digestion to the brain from the gut, and motor signals in the opposite direction. Research has shown a disruption of vagus nerve signalling in patients with anxiety and depression, signifying its importance (Cryan et al., 2019). This is referred to as neural signalling and is one of the ways in which the gut communicates with the brain. Another method is immune signalling. The gut hosts the largest immune organ in the body (Cleveland Clinic, 2025); gut microbes interact with the immune system, influencing levels of cytokines, which are signalling molecules that cause inflammation. Chronic, low-grade inflammation has been linked to depression and anxiety (Miller and Raison, 2016). Imbalances in the gut microbiota - called dysbiosis - can lead to inflammation that affects brain chemistry, which contributes to such mental health issues, as elevated levels of pro-inflammatory cytokines were found in patients of depression and chronic fatigue syndrome. Furthermore, chemical signalling plays a role just as relevant, as gut microbes help produce chemicals that directly or indirectly influence the brain, such as neurotransmitters: for example, 90% of the body's serotonin - which regulates mood, digestion and

sleep - is produced in the gut (Cleveland Clinic, 2025). GABA - a calming neurotransmitter, is produced by strains of lactobacillus (Bravo et al. 2011). Even dopamine, involved in motivation and reward, is affected by gut microbes. Research has also shown that lower levels of GABA are linked with higher anxiety, and changes in serotonin production in the gut can affect mood regulation. These pathways underpin emerging links between microbiota imbalances and neurological or psychiatric conditions, linking Parkinson's disease to gastrointestinal disorders like irritable bowel syndrome.

Recent Research into the Gut-Brain Axis

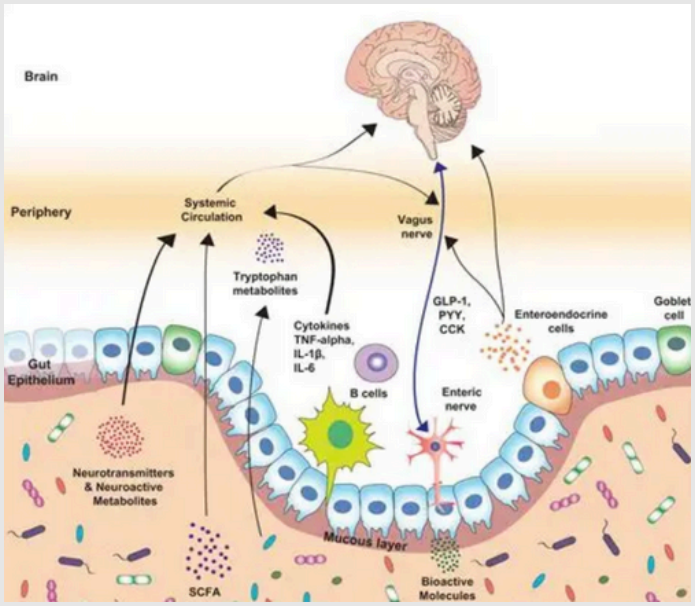

Figure 2. Gut microbiome (Cryan, 2019)

Recent studies have provided growing evidence that changes in gut microbiota can have a direct impact on brain function, mood and behaviour, through neural, immune and chemical pathways. A study conducted by UK and Australia-based research groups, published in BMC in 2024, investigated the strain-specific effects of probiotics on depression and anxiety. This meta-analysis reviewed 22 randomised controlled trials involving 707 participants, examining how strains of Lactobacillus and Bifidobacterium influenced mood (Smith et al., 2024). The research found a significant reduction in depressive symptoms when measured by the Beck Depression Inventory (BDI), although other scales did not show significant effects, highlighting the complexity of probiotic interventions. In addition, a study from Leiden University in the Netherlands, published in April 2025 (Johnson, 2025) suggested that probiotics can improve mood within weeks. 88 participants who took daily probiotics for two weeks experienced reduced anxiety, stress and fatigue, without the decrease in positive feelings often seen with conventional antidepressants. However, the researchers noted that these effects may involve shared pathways such as the vagus nerve but cautioned that probiotics should not replace conventional treatment. Furthermore, the Centre for Nutritional Psychology published a review in January 2025, summarising recent findings on microbial diversity, metabolites, immune signalling and neurotransmitter regulation. It highlighted the potential of microbiome-targeted therapies, including treatments such as personalised probiotics and dietary strategies, as complementary approaches to conventional mental health care. Collectively, these studies suggest that probiotics and dietary therapies hold real promise for the treatment of mental health issues, though findings remain complex and require years of further research and investigation.

Key Words:

Neurotransmitters:
chemicals that carry messages from nerve cells to other nerve cells, muscles, or other body parts

Parkinson's:
a disease of the nervous system that causes muscles to become stiff, movements to slow down, and the body to shake

Antidepressants:
a type of drug used to treat depression and other mental health conditions

Probiotics:
Live bacteria and yeasts that are beneficial for your body, particularly your digestive system

Evaluation and Implications for Medicine

Over the past decade, there has been an increase in research investigating the gut-brain axis, with both animal and human studies showing intriguing links between the composition of gut microbiota and mental health outcomes, including depression, anxiety, and cognitive decline. Studies have demonstrated that altering the gut microbiota through probiotics or dietary changes can influence behaviour and mood in animals, and to a lesser extent in humans. Unfortunately, the majority of such evidence comes from animal models, an example being germ-free mice that showed higher stress responses when transplanted with microbiota from anxious humans (Kelly et al., 2016). In contrast, human studies are often small in scale, short in duration and limited by variability in people's diet and lifestyle, meaning results may not be reliable, and promising results in animal models do not always translate to humans because of differences in physiology and behaviour. Moreover, the gut microbiome is as unique as a fingerprint, shaped by genetics, upbringing and diet (Cleveland Clinic, 2025). This overwhelming diversity means that it is impossible to ensure that a probiotic strain that benefits one person helps another, complicating treatment, and making it more expensive, as there is no standard prescription. Studies show people with depression may have different gut bacteria to others, but this may not prove that the gut bacteria actually change mood, as it could be equally argued that depression alters diet, which then effects the microbiome. This reflects the conflict of correlation and causation (Cryan et al., 2025). Mood and behaviour are often measured using self-reported questionnaires – which can only be subjective, so may not reflect the true effects of probiotics, whilst patients may be influenced by the placebo effect. Nonetheless, the future remains promising, as advances in metagenomic sequencing could allow doctors to specifically analyse an individual's gut microbiota and tailor treatments accordingly – selecting specific probiotic strains and dietary plans to improve mental and overall health (Marchesi et al., 2016). Such microbiome analysis could also be key in identifying early signs of depression, anxiety, autism spectrum disorders or even Parkinson's disease, also acting as a non-invasive screening tool so patients find it easier. Therefore, in the future, mental health care could include psychiatrists, microbiome specialists and dieticians, working together to address challenges. That said, there are valid concerns over the accessibility of such cutting-edge microbiome technologies and therapies, as it can be assumed they would initially be expensive, and difficult to implement in the NHS because of this unless significant investment is made. Moreover, it could take years for probiotics to be regulated safely across the world, with far more rigorous clinical trials required to ensure safety.

The gut-brain axis stands at the forefront of modern medical research, linking the gut microbiome to mental health in ways that are only beginning to be understood. While current evidence shows a strong link between the two, especially from animal studies, human research remains limited due to small sample size and doubts over true causes of behaviour. Nevertheless, the potential is immense, as targeted probiotics and dietary interventions could complement conventional treatments for depression, anxiety and neurodegenerative disease. However, at the moment, such methods should be seen as promising strategies for the future, requiring rigorous trials and regulation before integration into healthcare. This could allow for a more holistic approach to mental health care in the future. The gut-brain axis represents the interconnected nature of our bodies and suggests that the future of psychiatry lies as much in the gut as in the mind.

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TRINITY 2025

Why Does Drinking Tea Make Us Feel Better?

By Siyana Kotecha
(Year 13)

Key Words:

Overstimulation:
a state of being overwhelmed by too much sensory input

Placebo:
a harmless, inactive substance or procedure that looks like a real medical treatment but has no therapeutic effect

Tea is the second most widely consumed beverage globally, following water. Worldwide, it holds a significant cultural role across many societies, often symbolising hospitality and comfort. For instance, in China, tea is an integral part of traditional healing practices, symbolising purity and balance. Similarly, in the United Kingdom, the act of drinking tea is an important social custom, seen as an opportunity for bonding and relaxation. For the purpose of this essay, "tea" refers specifically to the infusion of leaves from the evergreen shrub Camellia sinensis, as opposed to pure herbal infusions. (Kosińska and Andlauer, 2014). This widespread consumption of tea raises an important question regarding its perceived capacity to influence our overall mood and happiness.

One of the most widely known benefits of tea consumption is that it makes us feel calmer. This is widely attributed to an amino acid derivative known as L-theanine. This has a similar structure to L-glutamate, shown in Figure 1.

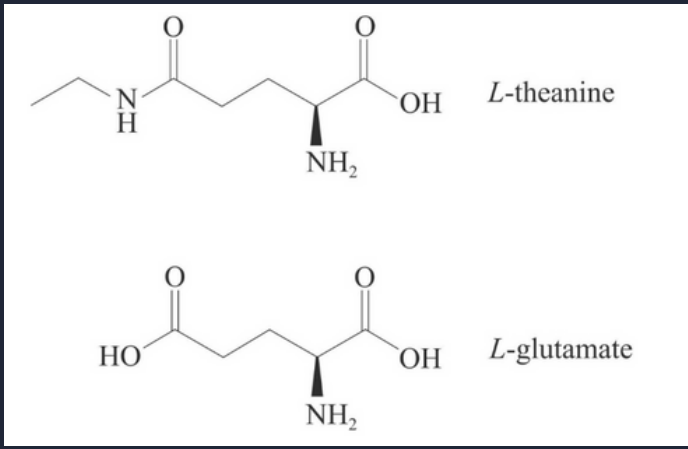

Figure 1. Chemical structure of L-theanine and L-glutamate (Wang et al., 2022)

As L-theanine has a similar structure to L-glutamate, it can block specific glutamate receptors and interact with the blood-brain barrier. (Wang et al., 2022). Glutamate is an excitatory neurotransmitter, which means it helps to transmit signals between neurones. (F. Lipnizki, 2010). When these glutamate levels are not balanced, it can lead to conditions such as depression, anxiety and stress. Imbalances in glutamate signalling have been linked to neurodegenerative conditions. (Kadbhane et al., 2021). Thus L-theanine, due to its structural similarity to glutamate, can bind to the specific glutamate receptors. This modulates the activity of glutamate, which maintains a healthy balance of excitatory signals in the brain itself, preventing overstimulation and encouraging calmness. (Wang et al., 2022).

L-theanine exerts its calming effects through both pre-synaptic and post-synaptic mechanisms. Pre-synaptically, it inhibits glutamine transporters, specifically the Slc38a1 transporter, which converts glutamine to glutamate. (Yoneda, Kawada and Kuramoto, 2020). By inhibiting this, it reduces glutamate levels, shown in Figure 2. Post-synaptically, L-theanine competes with glutamate at certain receptors such as AMPA, KA and NMDA receptors, which are involved in excitatory

signalling, impacting their functions. (Williams et al., 2019).

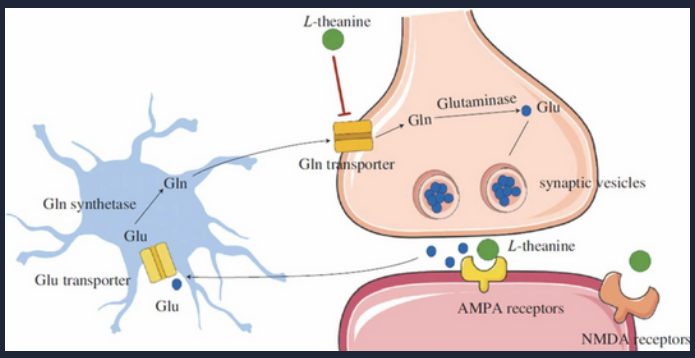

Figure 2. How L-theanine suppresses the glutamine transporter (Wang et al., 2022)

A second way L-theanine makes you feel calmer is by regulating Gamma-Aminobutyric acid (GABA) levels, however the exact pathway used is not fully understood. GABA is a chemical that reduces nerve cell activity, which therefore makes you feel more relaxed. Indeed, often, individuals with GABA abnormalities have mood disorders such as schizophrenia and bipolar disorder. (Duman, Sanacora and Krystal, 2019). For instance, a study by Yokogoshi et al. (1998) demonstrated that L-theanine administration increased GABA concentrations in certain regions of the brain, perhaps suggesting a potential pathway for its anti-anxiety effects.

The calming effects of drinking tea can be shown in some studies, and these effects are monitored using salivary amylase activity. The salivary amylase activity is a chemical marker sometimes used to assess psychological stress levels. When salivary amylase activity levels are higher, it is linked to increased psychological stress levels and activation of the sympathetic nervous system. Research by Unno et al., 2013 has shown that L-theanine can lower salivary amylase activity, indicating a reduction in the stress response. This was shown by the increase in the number of alpha waves in the participants' brains, which is associated with relaxed yet still alert states. In this study, participants who took a theanine supplement instead of the placebo showed significantly lower salivary amylase levels levels compared to the placebo group ($p=0.032$), which suggests that the results are statistically significant. Furthermore, subjective stress was significantly reduced in the group that took theanine ($p=0.020$). This means that taking theanine supplements helps to alleviate stress by reducing sympathetic nervous system activation. This highlights why drinking tea makes you feel better, as it naturally provides you with L-theanine, which potentially decreases your stress levels.

Catechins, particularly epigallocatechin gallate (EGCG), are powerful antioxidants found in tea that play a significant role in mood regulation. EGCG has been shown to trigger antidepressant-like behaviour in some animal models, particularly in rats exposed to chronic unpredictable mild stress (Li et al., 2020). The study demonstrated that EGCG alleviates depressive-like symptoms by reducing inflammation in the body, specifically through the inhibition of pro-inflammatory cytokines such as IL-6 and nitric oxide (NO), and by protecting neurons in the hippocampus. These findings highlight EGCG's potential as an anti-depressant by mitigating inflammation and promoting neuroprotection, supporting its role in emotional well-being (Li et al., 2020). As tea contains these catechins naturally, it could explain why drinking the beverage makes you feel better.

A simpler reason why drinking tea (or any hot beverage) makes you feel better could be due to the theory of social thermoregulation. This theory suggests that humans use social interactions and connections to help regulate their body temperature, by linking physical warmth with feelings of emotional warmth and social bonding (IJzerman et al., 2015). Indeed, primates seek to maintain thermoneutrality, which is essential for survival. Thermoregulation is a critical biological process because the human body functions

Key Words:

Neuroprotection:
a process or strategy that protects nerve cells (neurons) from damage, degeneration, or death

Thermoregulation:
the process by which an organism maintains its internal body temperature within a constant, narrow range, despite changes in the surrounding environment

optimally within a narrow temperature range, typically around 37°C. If the body's temperature deviates too far from this range, it can disrupt enzyme-controlled reactions and metabolic processes, potentially leading to physiological stress or even life-threatening conditions such as heatstroke or hypothermia. Therefore, maintaining a stable internal temperature is vital for sustaining cellular functions and overall health. In social contexts, physical warmth can act as a comforting signal, helping to reduce stress responses and promoting a sense of safety, which could further aid in the body's ability to regulate temperature in challenging environments. This interplay between physical warmth, social connections, and thermoregulation underscores why drinking tea not only provides comfort but also supports our biological well-being.

Research suggests that warmth is one of the most powerful traits in social judgement, with people automatically associating physical warmth with psychological warmth, such as trust and friendliness (Williams & Bargh, 2008). Early life experiences, such as physical warmth from caregivers (specifically mothers during breastfeeding), foster a lasting connection between warmth and comfort (Harlow, 1958; Bowlby, 1969). When core body temperature drops, humans crave warmth not only physically but also socially, making acts like drinking a warm beverage both physiologically and emotionally comforting.

Indeed, in a study from Yale University conducted by Williams and Bargh (2008) the relationship between physical warmth and social perceptions was investigated. This study was blind, and the forty-one participants were either given a cup of hot or iced coffee and thus exposed to physical warmth and coldness. Whilst the beverage used was not tea, the findings of the study are still applicable as the beverage used was not tasted, simply held. Following this, the participants were asked to describe the personality traits of a hypothetical person, Person A. Specifically, they were told that "Person A is intelligent, skilful, and industrious. Person A is also determined, practical, and cautious" (Williams & Bargh, 2008). Those who had held the hot coffee were significantly more likely to describe the person as having warmer, more caring and more generous traits in comparison to those who held the iced coffee. This highlights how the physical act of holding a hot beverage, namely tea, makes you perceive your surroundings and the people around you in a more positive way, thus making you feel better.

Moreover, a second study by IJzerman & Semin (2012) explores the connection between social exclusion and body temperature. Forty-one students participated in the video game "Cyberball", where they were either included or excluded within the game by other players. The participant and two other players toss a virtual ball back and forth, with the real participant receiving the ball every two throws in the inclusion condition. However, in the exclusion condition, the participant was intentionally ignored and did not receive the ball after the first two throws, simulating social exclusion. The results showed that the finger temperatures of the players who were included remained stable, whereas the finger temperatures of those who were excluded dropped. This suggests that social exclusion causes a literal drop in skin temperature. The second part of the study

explored whether inducing physical warmth could also alleviate the negative emotional effects of exclusion. Whilst playing the same game, players were exposed to either warm or cold tea. Excluded participants with the warm tea reported significantly lower negative affect compared to those with cold tea. This perhaps indicates that physical warmth can counteract the emotional negativity caused by distressing events such as social exclusion. Together, these studies highlight why tea makes you feel better as a physical warm drink can provide emotional relief and thus improve your mood.

To conclude, drinking tea can make us feel better through a combination of biological and psychological mechanisms, which is highlighted in the modern wellness movement as tea has seen a resurgence as a natural remedy for stress, anxiety, and even sleep disorders. The amino acid L-theanine plays an important role by regulating glutamate levels in the brain, helping to reduce stress. Moreover, its effects on GABA levels further contribute to its calming properties, as well as the catechins the tea contains potentially alleviating depressive like symptoms by reducing inflammation. The soothing nature of tea also extends beyond its chemical composition, with physical warmth linked to emotional comfort, as highlighted by the theory of social thermoregulation. Together, these factors demonstrate how and why tea has become a global symbol of comfort and relaxation, offering both a physical and emotional sense of well-being.

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TRINITY 2025

Quantum Cryptography: A Flawless Double Solution to a Millennia Old Problem and a New Security Threat?

Key Words:

Quantum:
the smallest possible amount of a physical quantity, such as energy, that can exist

Cryptography:
the practice of creating and understanding codes and ciphers to keep information secret and secure

Polarisation
the process of restricting the vibrations of a transverse wave, like light, to a single plane

Photon:
A particle of electromagnetic energy, such as light

By Kee Han Soh (Year 8)

The Basics

Quantum cryptography (also known as quantum encryption) refers to various cybersecurity methods for encrypting and transmitting secure data based on the naturally occurring and immutable laws of quantum mechanics (Schneider & Smalley, 2023). It is thus a theoretically unbreakable cryptogram. It has many variations; however, they all involve photons. The idea comes from the concept of quantum money, which is impossible to counterfeit (Singh, 1999).

Quantum Money & The Physics of Light

Photons are discrete packets of energy that make up light (Stark, 1999) and as a photon travels, it oscillates (vibrates) in one plane only – this is known as the polarisation of the photon (Singh, 1999). Wiesner's idea of quantum money, developed in the late 1960s, was to trap four polarisations of photons in banknotes: vertically polarised (90°), horizontally polarised (0°), and diagonally polarised (45° and 135°). If we put a Polaroid (a type of filter) in the path of some photons, we can make sure that the photons that pass through all vibrate in the same direction (i.e. they all have the same polarisation) and therefore any photon that is already polarised at the same angle as the Polaroid's optic axis will pass through. However, photons which were polarised 45° to the optic axis of the Polaroid would have a ½ chance of being twisted and having its polarisation changed to match that of the Polaroid's optic axis (Bennett et al., 1992). This is where Wiesner came in: he had the idea to trap a series of photons with specific polarisations in a banknote. The banker checks the photons in the bank note using the corresponding Polaroids to check to see if they are in the correct polarisation. If some of them do not pass through, the banker knows that it has been tampered with or is counterfeit. If, however, all of the photons pass through, the banker has validated the banknote and fills the traps with correctly polarised photons. The counterfeiter does not know which Polaroids to use and therefore cannot measure the polarisations of the photons reliably. Say the counterfeiter uses a 0°

Polaroid to measure the first photon. If the photon does not pass through, there is a problem: is the photon polarised at 45°, 90°, or 135°? Say the counterfeiter then uses a 45° Polaroid for the second photon. This time, the photon passes through at 45°; however, was the original polarisation 0°, 90°, or 45°? The struggle to accurately measure photons was studied by German physicist Werner Heisenberg, whose 1927 paper "The Actual Content of Quantum Theoretical Kinematics and Mechanics" explains that we cannot know all of its properties at one point in time, e.g. we cannot simultaneously know the precise position and velocity of an electron. Therefore, we cannot know with certainty the velocity or the direction of oscillation of the photon when it reaches the Polaroid. Quantum money was a novel idea, taking advantage of quantum mechanics: why was it not implemented? The answers are simple. Firstly, we do not have the technology to trap photons in a specific polarised state for a sufficient amount of time to render it practical. Even if we could (and that is a big if), it would be extremely expensive to maintain each banknote (Singh, 1999). It is currently not practical.

The Theory Behind Quantum Cryptography

For years, Wiesner struggled to get his paper published by scientific journals. He felt that no one was appreciating the idea and people did not understand the physics (Singh, 1999). He then turned to his old friend of his: Charles H. Bennet, who was intrigued by it. Bennet then pondered over the concept and thought about whether it would have a more practical application. While attending a conference in San Juan, he saw that a Canadian computer scientist by the name of Gilles Brassard was going to deliver a talk concerning cryptography. Thinking that Brassard might be interested in Wiesner's ideas, he told Brassard about quantum banknotes (Gregersen, 2024). Both were fascinated with the concept and together they developed the first quantum cryptography scheme: BB84, which had their initials followed by the last two digits of the year it was conceived, 1984. It became known as Quantum Key Distribution, or QKD, where a quantum cryptographic system would be used to safely transmit a secret key between two people (Bennett et al., 1992). Let us use the same example used in Bennet, Brassard, and Ekert's paper on Quantum Cryptography in 1992: there are two people trying to communicate and they are called Alice and Bob. Alice wants to send an encrypted message to Bob. For symmetrical ciphers, the same key is used to encipher and decipher a message therefore both parties have to know what key will be used so that the transmitter can encipher a message and that the recipient can decipher it (Badman & Kosinski, 2024). The only mathematically impossible cipher to decipher without the key is a type of symmetrical cipher, namely a one-time pad (OTP) cipher and an OTP, if done properly, is virtually unbreakable (CIA, 2021). According to Crypto Museum (2015), the key follows five rules:

- The key should be made of completely random characters.
- The key should have the same length as the plaintext (or longer).
- Only two copies of the key should exist.
- The key should be used once and only once.
- Both copies of the key should be destroyed immediately after being used.

Key Words:

Oscillation:
a regular, repetitive movement back and forth or up and down around a central point

Encrypted:
to have information, especially digital data, converted into a secret code

Symmetrical Cypher:
an encryption method that uses the same secret key for both encrypting and decrypting information

It can get impractical for Alice to inform Bob of the key as it is so long, and it has to be kept absolutely secret to be secure. This is where quantum key distribution steps in. QKD allows Alice to transmit the key in binary to Bob in absolute privacy. The method involves using a transmitter and a receiver and is based on the same principles of polarised light discussed in the previous section. First, Alice uses the transmitter to send photons which are polarised at 0, 45, 90, or 135 degrees where 0 and 135 degrees means '0' and 45 and 90 degrees means '1'. Bob, on the receiving end, has two options with the receiver. The receiver can characterise between rectilinear polarisations or can be rapidly changed to differentiate between diagonal polarisations. Note that it can never distinguish both types at the same time. Since Bob does not know what photons Alice sent, he switches between the two configurations randomly. After Alice has finished sending photons and Bob has finished trying to detect Alice's photons, Bob then tells Alice what configuration he used to try to detect each photon. Alice then confirms whether Bob used the correct configuration (and the received photon becomes the next digit of the key) or whether Bob got it wrong (in which case both Alice and Bob would discard that photon's digit and not use it in their key). This way, at the end both parties will have the same key and encryption can follow (Bennett et al., 1992).

The Unbreakable Cipher?

Now, let us introduce a new character: Eve, who is trying to intercept the key to decipher the message that will follow. Like Bob, Eve does not know what scheme (rectilinear or diagonal) Alice used for the photons sent. To obtain the same key as Alice and Bob, Eve needs to somehow choose the same schemes (or at least most of them) as Bob to have a chance of deciphering the message later. To make matters worse, when Eve intercepts the photon with the wrong scheme, Eve has a ½ chance to cause the photon to 'twist' and affect the results that Bob detects. For example, say Alice sends a photon polarised at 0°. Bob then uses the correct configuration, rectilinear, and detects 90°. There has obviously been interference, whether that be someone trying to intercept the key (like Eve) or other sources, though we can deduce that devices designed for QKD therefore try to minimise these interferences to ensure accuracy of the transmission and the resultant key. To prevent Eve possibly listening undetected, Alice can confirm with Bob several of the digits of their key and discards them. If there is a discrepancy, Alice and Bob will assume someone such as Eve has intercepted some of their photons and they will have to start the process over again on a different connection. The chance of Eve not affecting Bob's measurement of 75 random photons taken from a 1075-digit key in binary is less than 1 in a billion (Singh, 1999).

Quantum Key Distribution: Issues and Solutions

Even this method of verifying by comparing photons is inefficient, sacrificing too many digits of the key. Instead, Alice and Bob can compare random subsets by comparing whether the number of '1's there are in the subset is odd or even (known as the parity).If Alice's and Bob's data has a discrepancy, comparing the parity of a random subset will detect that fact with a probability of 1/2, regardless of the number and location of errors (Bennett et al., 1992). We can work out, using a calculator, that by repeating this process 20 times with different random subsets, we reduce Eve's chances of going undetected from 1 in 2 to 1 in 220 which equals to 1 in 1048576. This method allows for sufficient chance that Eve will be detected without compromising a lot of digits of the key which then have to be discarded. The first prototype built for a QKD exchange used flashes of light instead of photons. This, however, allows a particularly cunning Eve to use a half-silvered mirror to split the flash of light into two halves of lesser intensity and attempts to detect one of

the halves whilst allowing the other to reach Bob without interference and therefore evade detection. This can be solved by having Alice send very dim flashes of light (like in the prototype where each flash was on average one tenth of a photon), however, this slows the rate of data transfer (Bennett et al., 1992). Since the construction of a prototype by Bennett and a research student John Smolin which had the transmitter and receiver separated by 30 cm, the goal had been to find a way build a quantum cryptographic system that can work over long distances which is not trivial because photons do not travel well (Singh, 1999). If a polarised photon is sent via air, the air molecules in the air could potentially change the polarisation and skew the results. An alternative is to use optic fibre and recently according to Pittaluga et al. (2025) scientists in Germany have managed to implement the coherence-based twin-field QKD protocol over a 254-kilometre commercial telecom network spanning between Frankfurt and Kehl, Germany, achieving encryption key distribution at 110 bits per second without using cryogenic cooling. This shows that quantum cryptography can now be used over large distances via already exiting optic fibre networks.

Conclusion

Quantum cryptography solves the issue of secure key distribution (a millennia old problem) and combats the threat of quantum computers (a new threat). It is unbreakable, a big claim in the light of earlier ciphers such as the German Enigma cipher which was believed to be unbreakable until it was broken, however, quantum cryptography is truly unbreakable according to the laws of quantum physics. If it is ever broken, that would mean that physicists would have to reconsider the fundamental laws of physics (Singh, 1999). It is, to the best of our knowledge, secure.

Key Words:

Rectilinear:
moving in or forming a straight line

Discrepancy:
a difference between two things that should be the same

Coherence:
the quality of being logical, consistent, and making sense as a connected whole

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Key Words:

Antibiotics: medicines that kill or stop the growth of bacteria to treat infections

Intravenous: into or connected to a vein, especially for giving drugs or food

Microbiome: the community of microorganisms (such as bacteria, fungi, and viruses) that live in a particular environment, especially in the human body

Faecal: relating to or consisting of solid waste passed from the body

TRINITY 2025

The Might of Microbes: How Faecal Microbiota Transplantation Turns Waste into Cure

By Prakash Easwar (Year 12)

In the fourth century, long before antibiotics and intravenous drips were discovered, a Chinese researcher, Ge Hong, faced a great medical challenge when treating patients with severe food poisoning and awful diarrhoea. With no magical modern medications available to treat the disease, Ge Hong turned to a rather unconventional family remedy - which he called his 'special yellow soup'. Unlike your grandmother's comforting chicken broth, this ancient concoction had a secret ingredient that was, quite literally, bottom shelf: faeces. Yes, centuries before clinical trials and double blinded studies, Ge Hong was conducting the earliest version of what we call now a faecal microbiota transplant (FMT) - a gut feeling that turned out to be scientifically spot on.

The Role of the Microbiome in Immunity

In order to understand why FMT is so effective in treatment, we must first understand what our microbiome is - and why it matters.

A microbiome is an entire community of microorganisms (bacteria, viruses, fungi, and their genes/metabolites) that live in an in environment, like your skin, gut, or lungs, along with their activities and interactions. Most of the human microbiome is in the gut - specifically the large intestine.

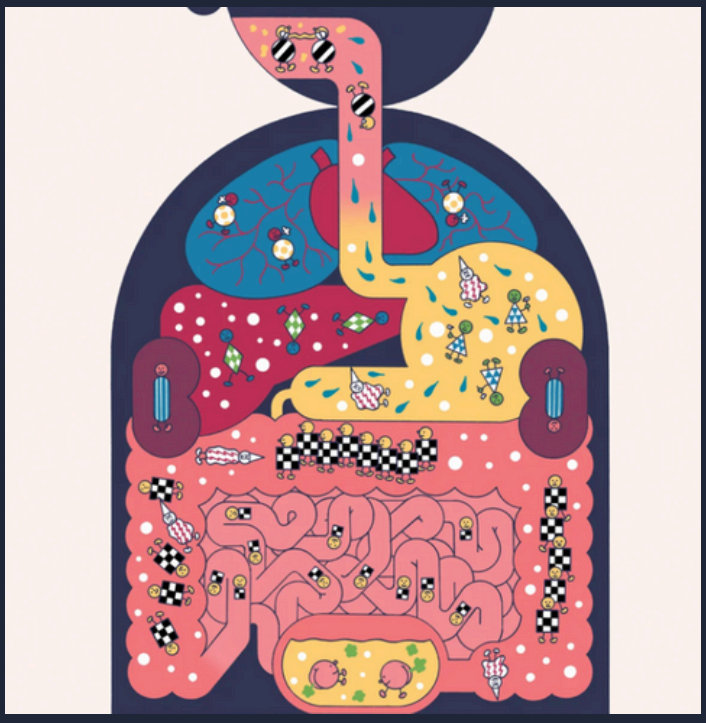

Figure 1. (The Guardian, 2018)

The large intestine is lined with intestinal epithelial cells (IECs) and contains lots of white

Key Words:

Homeostasis:
the process by which a living organism maintains a stable internal environment despite changes outside

Fermentation:
the chemical breakdown of substances by microorganisms, often producing gases, alcohol, or acids

blood cells, both of which the microbiome interacts with to maintain gut homeostasis; they all together help digest food, outcompete other pathogens, and shape immune responses. But let's now focus on the microbiome's crucial role in regulating our immune system. Our immune system can be separated into the innate and adaptive immune system. The innate immune system is a non-specific general defence to pathogens, with a quick response speed but no memory - consisting of the Phagocytes, Neutral Killer cells and dendritic cells. They try and kill all the unknown invaders entering the body. However, the adaptive immune system is much more specific to the pathogen. It consists of the B and T cells. The B cells produce antibodies, and T cells either target and kill infected/abnormal cells (cytotoxic T cells) or coordinate other immune cells (helper T cells). The microbiome causes effects on the B and T cells (the adaptive immunity) - including driving the balance between T helper cells and T regulator cells (the cells which regulate inflammation). Specifically, segmented filamentous bacteria in the microbiome promotes T helper 17 cells to be produced, which are very important in promoting inflammation and fighting extracellular pathogens - especially fungi. (Ivanov et al., 2009).

Another bacteria in the microbiome, Bacteroides fragilis, produces a special molecule called Polysaccharide A which tells the immune system to calm down. This helps increase T reg cells, as they control the amount of inflammation. Both of these good bacteria cause B cells to change the type of antibody they make, which is very important for long-term peacekeeping in the body. They cause something called class switching, where B cells change from producing IgM, the first clumsy and inflammatory antibody your body makes when it sees something new, to IgA, a specialised and more precise antibody for lasting protection at mucosal surfaces like the gut or lungs. So, in short, our microbiome plays a crucial role in our adaptive immune system by regulating the amount of inflammation, and making the antibodies produced to be more specific and effective.

How To Change Your Microbiome

But what is so empowering is that we can make our immune system stronger and cultivate a better microbiome through what we eat.
Since we have trillions of microorganisms in our microbiome, we have so many different species of microorganisms that feed off different foods. Some microorganisms, thrive off highly saturated fats - like those in our urban diets of McDonalds and Burger King. The saturated fats these diets contain increase the levels of an acid called taurocholic acid in your body, which often lets the bad bacteria in your microbiome thrive. As the population of bad bacteria consequently increases and increases you now have more bad bacteria than good bacteria, and the balance of bacteria is skewered - this is known as dysbiosis. You constantly crave more high fat foods, since the high population of bad bacteria need it to survive. Since the population of good bacteria in your microbiome has decreased, you can't fight off infection and absorb vital nutrients (Devkota et al., 2012).

However, you can force the right kinds of microorganisms to grow by eating the right kinds of food. Other good microorganisms thrive in fibre-rich environments. When we eat a high fibre diet, the good bacteria thrive and converts fibre into short chain fatty acids (SCFA's) through

fermentation. SCFA's are an important nutrient source for the intestinal epithelium and helps to shape it — meaning more vital nutrients are absorbed. Moreover, short chain fatty acids help produce more T Reg cells (Hu M et al. 2022), which as mentioned before dampen down the immune system and reduce inflammation, but SCFA's also enhance cytotoxic T cells' function. This is crucial for antiviral and anticancer immunity. What's more, an increase in the population of good, fibre-focussed bacteria causes a decrease in a bad bacteria that is linked to obesity and metabolic disorders (called Firmicutes). Therefore, eating fibre is essential to cultivate the right bacteria in our microbiome; this is why eating a mainly vegetarian diet is seen as helpful for our immunity.

But it is also important when you eat your food, not just what you eat. It is thought that intermittent fasting (having regular patterns of when you eat and when you fast) helps the microbiome promote the right bacteria. This again helps produce more T regulator cells, and moderates the balance of microorganisms in your gut. (Cignarella et al. 2018). So, changing when you eat helps strengthen your immune system too!

Antibiotics and Clostridium Difficile

Now I have given you some sort of context on the interplay of the microbiome and the immune system, we are now going to focus on how antibiotics can cause change in our gut microbiome — and how FMT works to counteract it. Often antibiotics are used to treat patients with bacterial infections, and their introduction has dramatically changed healthcare and increased life expectancy. However, Antibiotics mess up the composition of the gut microbiota as they kill bacteria indiscriminately in your colon. While they do have the positive effect of killing the harmful bacteria, they also kill the good bacteria in your colon (that we have established is good to fight infection and aid digestion). This helps create a niche in your colon for the bad, resistant bacteria to grow and divide — as there are no good bacteria to outcompete them.

A similar effect is caused by Inflammatory Bowel Disease (IBD), an autoimmune disease where the immune system attacks its own gut tissues, causing chronic inflammation and reduced microbial diversity as the microbiome cannot happily live there — again creating a niche for harmful, resistant bacteria.

Figure 2. (Rohde, n.d.)

The name of the bacteria in the colon that thrives in this harmful niche, is Clostridium Difficile, often called C. diff. Every one of us has C. diff in our colon right now, but most of us have the right balance of C. diff with good bacteria. Since antibiotics (and IBD) cause an imbalance of microorganisms in the microbiome, there is less competition for nutrients and heat, and so C Diff thrives. But it doesn't have to be you taking the antibiotics to get C. diff — C. diff infections spread easily, most often in hospitals, long-term care facilities, and other buildings — where people are sick or in a weakened state. It takes over by forming spores in the colon that can become immune to antibiotics and difficult to destroy — causing real internal upset. C Diff releases exotoxins A and B, with A causing prolonged watery (and painful) diarrhoea, and B causing pseudo membrane colitis (a life-threatening, painful condition where the GI tract rips open and all the toxic substances present inflame your internal organs, leading to death unless immediate treatment). It also generally leads to lower levels of short-chain fatty acids

Key Words:

Coprophagy:
the eating of faeces, especially by animals as part of their normal behaviour or diet

bidirectional communication:
communication that flows in both directions, allowing exchange and feedback between parties

(SCFAs) in the gut for your intestinal lining, so it really is an awful disease — and for a long time there were very few treatment options!

Ironically, the original treatment was antibiotics, which targeted C. diff directly, but this also furthered the damage to the gut microbiota, which helps C. diff persist or return — especially after repeated use. After this treatment, about 20-30% of patients experienced relapses, and after several relapses the chances of long-term recovery using antibiotics alone drop dramatically. This led to a vicious cycle of antibiotics, temporary improvement, relapse and then more antibiotics. Doctors tried probiotics to restore gut flora and eventually some C Diff patients had to even go under a subtotal colectomy — a high risk, drastic surgical measure with high mortality rate. It wasn't until in America in 1958, when American physicians used a modern version of Ge Hong's ancient yellow soup to treat pseudomembranous colitis (which we now know was C. Diff) that the prospects of C Diff patients ameliorated.

Faecal Transplantation

Poo. Who would have thought it? When all other drugs failed, Ben Eiseman and his colleagues in Colorado turned to faeces to treat four critically ill patients. But I'm sure you're wondering how faeces can help restore the microbiome when it has been destroyed by antibiotics or IBD. I have reiterated the importance of microbial balance and good microbial diversity — but when the faeces have entered the gut its own microorganisms recolonise and reseed the colon, outcompeting harmful bacteria like C. Diff. This helps restore the gut barrier and immune function, as those SCFA's I talked about are restored, nourishing the gut lining, and the inflammation caused by pseudo membrane colitis is reduced through the microbiome stimulating more T Reg Cells. C. diff thus loses its ecological niche and is eliminated. So, in simple terms, it replaces the bad bacteria with good bacteria — resetting your microbiome and giving your gut a second chance.

Figure 3. (Cary Gastro, 2024)

This concept is actually very natural, with many animals doing it regularly to survive (known as coprophagy) — and it is much simpler than synthesising any antibiotic. You find a healthy, screened donor, then take a frozen stool sample and mix it with liquid, filter to concentrate bacterial portion, and then give the bacteria to the sick person. 80% of C Diff and other Microbial diseases are cured in one faecal transplant for these sick patients, proving it better than the best IV immune-suppressant drugs, and without risk of cancer and adverse events.

But despite the process seeming very straightforward, choosing an adequate donor is very rigorous; less than 5% of those who apply to be a stool donor are actually accepted. Since stool contains very many potentially harmful pathogens, donors have to test negative for a wide range of infectious diseases via blood and

stool testing. The microbiome quality also must be optimal, having a rich diversity of microbes to ensure that good bacteria will take over. To prevent unknown risks donors are rejected for recent antibiotic use, chronic gastrointestinal conditions, metabolic/psychiatric disorders, and a family history of autoimmune, metabolic, or neurodevelopmental conditions.

Yet, FMT is still very much an experimental treatment because of the wide interplay of the microbiome. One patient has died from FMT after E Coli unknowingly being transferred, and it is thought that the wrong donor can cause the patient to have a greater risk of obesity, and it may even be able to contribute to personality disorders and mood swings. It is for these reasons that very few doctors even nowadays use FMT and instead opt for very strong antibiotics like vancomycin and fidaxomycin to treat Clostridium Difficile.

You may be wondering how a change in gut microbiome can affect things in the brain, like your personality. Well, in our body, we have a gut-brain axis: a bidirectional communication network between the gastrointestinal system and CNS — strongly influenced by the gut microbiota. When a faecal transplant is introduced, and the person's microbiome now has a different composition, it can lead to new neuroactive metabolites forming (like Dopamine) which will affect sensory processing, social behaviour, and stress sensitivity in the brain. John F. Cryan and Ted Dinan in 2012 found that when transferring microbiota from anxious/depressed mice, it induced anxious or depressive-like behaviour into mice that didn't originally have it. Another group in Ireland in 2016 found that anxiety could be transferred through FMT due to the interplay of the microbiome in rats. So, it is essential that precautions are taken to minimise any risk of induced behavioural changes in FMT, and that FMT remains largely experimental until we fully understand the complex interplay of the microbiome.

The Future of FMT

However, the future of FMT is still very exciting. It is thought that FMT in the future might be able to ameliorate behavioural and physiological abnormalities, due to the interplay of the microbiome. Hsiao et al. in 2013, found that in a mouse model of autism, FMT improved the mouse's social behaviour and communication with other mice (due to new neurotransmitters forming). Autism has no cure, and only management — but transferring poo was shown to make mice less socially anxious and could be a possible treatment method.

Moreover, FMT has even shown results in treating diabetes and cancer. When treating type 2 diabetes, FMT helps **r**epopulate the gut with beneficial microbes that improve insulin sensitivity, reduce inflammation, and regulate metabolism. It works by rebalancing the gut microbiome-metabolism-immune axis, and has shown results in mice, where faecal transplants from non-diabetic mice improved insulin resistance in mice with type 2 diabetes (Chen L et al. 2023). Since FMT strengthens your immune system by increasing the number of WBC's (Reinvigorating exhausted T cells), it is used to treat cancer by activating T cells that migrate to the tumour and destroy cancer cells.

Faecal microbiota transplantation is currently an experimental, yet effective treatment method against Clostridium Difficile — an infection predisposed by inflammatory bowel disease, and prolonged use of antibiotics. It works by rebalancing the microorganisms in our microbiome, when bad bacteria have taken over, kicking out all the bad bacteria. The FDA still classifies FMT as experimental since we don't completely understand the microbiome's complete interplay within the body. But this makes FMT very exciting, being a possible, and highly probable cure to autism, type 2 diabetes, and cancer in the future.

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TRINITY 2025

The Fast Lane for Weight Loss: Does Intermittent Fasting give Ozempic a Run for its Money?

By Yahya Musa (Year 13)

Key Words:

Semaglutide: a medication that mimics natural gut hormones to help regulate blood sugar, slow digestion, and reduce appetite

Obesity: the condition of having excess body fat that may impair health and increase the risk of disease

Pharmacotherapy: the treatment of disease through the use of pharmaceutical drugs, often as part of a broader medical approach

The global surge in obesity and type 2 diabetes has prompted researchers, clinicians and the public to seek effective, sustainable interventions for weight management and metabolic health. Although pharmacological treatments such as Ozempic (semaglutide) have attracted widespread attention for their rapid improvements in glycaemic control and weight loss, concerns remain about unwanted side effects, cost and long-term dependency (Wilding et al., 2021). In contrast, intermittent fasting—a cyclical approach to eating that alternates periods of consumption with abstention—has re-emerged as a natural, cost-effective strategy that aligns with our evolutionary design. This essay explores the scientific basis of intermittent fasting, its benefits for weight loss and diabetes management, and compares it to Ozempic, ultimately suggesting that our ancient metabolic rhythms may hold the key to enduring health.

Obesity and Type 2 Diabetes: The Modern Epidemic

Obesity and type 2 diabetes are not merely individual health issues; they are systemic challenges that strain healthcare systems worldwide. Sedentary lifestyles, highly processed diets and genetic predispositions have all contributed to disrupted metabolic functioning, resulting in elevated blood glucose levels and chronic insulin resistance (Petersen and Shulman, 2018). The World Health Organisation (2020) stresses that obesity is far more than an aesthetic concern—it is a public health crisis that increases the risk of heart disease, stroke and other serious metabolic disorders.

Traditional approaches have largely centred on calorie restriction, regular exercise and, when warranted, pharmacotherapy. Medications like Ozempic are designed to modulate hormonal pathways and target hyperglycaemia. However, despite the measurable benefits, issues such as side effects and cost have driven the search for additional, more holistic solutions. Intermittent fasting has gained renewed focus as a method to recalibrate the body's metabolic machinery and tackle the root causes of these epidemics.

Ozempic: Promises and Pitfalls

Ozempic, a glucagon-like peptide-1 (GLP-1) receptor agonist, is widely recognised for its role in enhancing insulin secretion and curbing appetite, thus effectively lowering HbA1c levels

and promoting weight loss (Wilding et al., 2021). Originally developed to help patients with type 2 diabetes manage glycaemic control, its rapid and noticeable effects have led to a broader appeal. In recent years, the drug has attracted significant attention beyond medical circles, with numerous celebrities and social media influencers endorsing it as a "miracle cure" for weight loss. Such endorsements often highlight dramatic results, fuelling a trend that positions Ozempic as the go-to solution for those seeking a quick fix, regardless of whether their primary issue is diabetes or obesity.

However, the increasing popularity of Ozempic comes at a cost. Many users report adverse effects ranging from severe nausea, vomiting, and diarrhoea—which in turn can lead to dehydration and intense abdominal discomfort. More alarmingly, there have also been case reports of acute pancreatitis and gallbladder dysfunction, including an increased risk of gallstone formation and cholecystitis (Drucker, 2024). These side effects, while not universally experienced, raise significant concerns about the long-term safety of chronic GLP-1 receptor stimulation. Alongside its side-effect profile, the high cost of the medication and the need for consistent medical supervision further compound the challenges, making it less feasible for widespread, unsupervised use.

The aggressive promotion of Ozempic by celebrities and on social media platforms exacerbates these concerns. By showcasing only the rapid weight-loss benefits, these endorsements can create an overly optimistic view of the drug, encouraging individuals to seek it out as a shortcut without fully understanding the potential risks. This celebrity-driven hype can lead to misuse or unsupervised adoption of the medication, sometimes bypassing necessary medical consultation. Ultimately, while Ozempic offers genuine clinical benefits for many patients, the emphasis on its "miracle" effects in popular media can overshadow the serious safety concerns and lead to a public misunderstanding of its appropriate use, underscoring the need for more balanced and evidence-based health communication.

Key Words:

Pancreatitis:
inflammation of the pancreas, often causing abdominal pain and digestive problems

Autophagy:
the natural process by which cells break down and recycle their own components, helping to remove damaged parts and maintain cellular health

Fasting: Historical Roots and Modern Resurgence

Fasting is an ancient practice embraced across diverse cultures and religious traditions for both spiritual purification and physical wellbeing. In Islam, fasting is especially revered as part of the tradition of Sawm, where adherents abstain from food, drink, and other physical needs during daytime in the month of Ramadan. This rigorous fast not only cultivates self-discipline and gratitude but is also associated with a range of health benefits, such as improved metabolic markers and enhanced mental clarity.

While few religions observe fasting as stringently as Islam—with its completely nil-by-mouth approach for most of the day—many other faiths integrate the practice into their spiritual life. In Christianity, for example, fasting is a key component of Lent, a 40-day period of penitence and self-reflection. Similarly, Judaism features fasting as an essential observance on Yom Kippur, the Day of Atonement, to purify the soul and seek forgiveness. Hindu traditions also incorporate fasting, with practices such as observing Ekadashi—fasting on specific days each month believed to cleanse both body and spirit. These varied traditions underscore fasting's enduring role in supporting both spiritual growth and physical health, affirming its value across different cultures and epochs.

Across these traditions, fasting has historically served purposes that extend beyond the spiritual realm. Whether as a way to sharpen focus, detoxify the body, or cultivate resilience, fasting underscores a universal human connection to cycles of nourishment and abstention. In modern times, scientific research has validated many of these traditional practices, illustrating how intermittent fasting can significantly improve metabolic health, promote weight loss, and reduce inflammation (de Cabo and Mattson, 2019). Contemporary approaches—such as time-restricted feeding (e.g., the popular 16/8 method), alternate-day fasting, and the 5:2 regimen—allow individuals to integrate fasting into daily life while reaping its broad physiological benefits (Longo and Panda, 2016).

The Physiology Behind Fasting

Intermittent fasting sets in motion a series of beneficial processes that extend well beyond simple calorie restriction:

Enhanced Insulin Sensitivity

Extended periods without caloric intake force the body to utilise stored energy. This process results in lower circulating insulin levels and improves cellular responsiveness, directly countering the chronic hyperinsulinaemia seen in metabolic syndrome (Petersen and Shulman, 2018).

Induction of Ketosis

With limited glucose availability, the body shifts to burning fat for fuel, producing ketone bodies. Ketosis is not only a survival mechanism—it is linked to improved energy efficiency, reduced inflammation and neuroprotective effects (Moro et al., 2016).

Activation of Autophagy

Fasting promotes autophagy, a cellular recycling process in which damaged organelles and proteins are broken down and repurposed. This self-cleansing mechanism is associated with a reduced risk of chronic diseases, including neurodegenerative disorders and some cancers (de Cabo and Mattson, 2019).

Hormonal Regulation

Periods of fasting trigger beneficial hormonal changes. Reduced insulin is paired with higher levels of glucagon and growth hormone, which not only aid in fat oxidation but also help to preserve lean muscle mass (Longo and Panda, 2016).

Together, these processes demonstrate that intermittent fasting re-sets the body's metabolic pathways and promotes a more robust, resilient physiological state.

Comparing Efficacy in Weight Loss and Metabolic Health

Both Ozempic and intermittent fasting produce significant weight loss and improved metabolic markers, though they do so via different routes. Ozempic produces rapid benefits by pharmacologically stimulating satiety and insulin secretion (Wilding et al., 2021). Intermittent fasting, however, taps into the body's innate capacity for energy regulation—inducing ketosis, activating autophagy and orchestrating hormonal shifts that lead to sustained weight loss and enhanced insulin sensitivity (de Cabo and Mattson, 2019). In many studies, intermittent fasting has yielded weight loss outcomes comparable to traditional calorie-restricted diets, often accompanied by additional cardiovascular benefits and reduced inflammation (Tinsley and La Bounty, 2015).

Safety, Sustainability and Economic Considerations

When comparing safety and long-term sustainability, the approaches diverge significantly. Ozempic's side-effect profile—from mild gastrointestinal discomfort to more severe complications—can undermine its long-term use (Drucker, 2024). Its high cost and reliance on

continual medical oversight further limit its accessibility. By contrast, intermittent fasting is a natural, virtually cost-free intervention with minimal risks when practised correctly. While not suitable for everyone—for instance, individuals with certain eating disorders or advanced diabetes must proceed with extra caution (Antoni et al., 2017)—its overall benefits and ease of integration make it an attractive option for long-term metabolic management.

Fasting in the Context of Diabetes Management

For those with type 2 diabetes, achieving optimal glycaemic control is essential. Intermittent fasting has been shown to reduce basal insulin levels and improve insulin sensitivity, thereby regulating blood glucose more efficiently (Petersen and Shulman, 2018). Clinical studies have demonstrated that patients who adopt fasting protocols experience significant improvements in HbA1c and overall glycaemic control compared to those on conventional diets (Moro et al., 2016). In addition, by promoting a metabolic shift from carbohydrate dependence to fat burning, fasting alleviates the inflammatory and oxidative stresses that commonly exacerbate diabetic complications (Antoni et al., 2017). This dual action—regulating blood sugar and reducing cardiovascular risks—renders intermittent fasting a promising complement to standard diabetic care.

Integrating Fasting into Daily Life

The practical success of intermittent fasting depends on its adaptability to individual lifestyles. Popular regimens include the 16/8 method, where one fasts for 16 hours and eats within an 8-hour window, and the 5:2 approach, which involves severe caloric restriction on two non-consecutive days each week (Tinsley and La Bounty, 2015). For beginners, it is advisable to start with shorter fasting periods and gradually extend the duration, ensuring that nutrient-dense foods—rich in whole grains, lean proteins, fruits, vegetables and healthy fats—are consumed during feeding times (Longo and Panda, 2016).

Key Words:

Glycaemic:
relating to the presence or level of glucose (sugar) in the blood, often used in contexts like glycaemic index or glycaemic control in diabetes management

Emerging research also indicates that intermittent fasting may yield cognitive and psychological benefits. Increased levels of brain-derived neurotrophic factor (BDNF) during fasting are linked with improved memory, enhanced mood and greater mental clarity (Mattson et al., 2017). In today's fast-paced world, the neuroprotective effects of fasting add yet another layer to its overall appeal—highlighting its potential role in cultivating both physical and mental resilience.

Future Directions and Weighing the Options

The science behind intermittent fasting is dynamic and evolving. Researchers are now investigating the interplay between fasting, circadian rhythms and gut microbiota, aiming to develop custom-tailored fasting regimens that account for genetic and lifestyle differences (Longo and Panda, 2016). Longitudinal studies are also in progress to assess the long-term impacts of sustained fasting on ageing, cognitive function and chronic disease progression. Such insights could help integrate intermittent fasting into broad public health strategies and personalised care protocols.

Deciding between a pharmaceutical intervention like Ozempic and a lifestyle modification such as intermittent fasting does not have to be an either/or proposition. While Ozempic can deliver rapid improvements in glycaemic control and aid in short-term weight loss, its drawbacks in terms

of side effects and cost suggest that a more sustainable, holistic approach may be preferable in the long run. In many instances, a combined strategy—using short-term pharmacotherapy to jump-start metabolic improvements alongside a transition to intermittent fasting—may offer the most balanced and enduring outcomes (Inzucchi et al., 2012).

Conclusion

The escalating challenges of obesity and type 2 diabetes compel us to explore holistic, evidence-based strategies that extend beyond conventional pharmacotherapy. Although Ozempic demonstrates impressive efficacy in reducing blood sugar and promoting weight loss, its adverse effects, expense and long-term uncertainties underscore the need for alternative approaches. Intermittent fasting—steeped in ancient practice and now validated by modern research—not only improves insulin sensitivity and promotes cellular repair but also realigns our metabolic rhythms in a way that supports both physical and mental well-being.

As investigations into nutritional timing, cellular autophagy and circadian biology progress, intermittent fasting is poised to become a cornerstone of personalised healthcare. Whether used as a standalone method or in combination with targeted medications, this natural intervention invites us to reconnect with our evolutionary heritage and embrace a lifestyle that is sustainable and profoundly beneficial. Ultimately, the choice is ours—to rely solely on short-term fixes, or to adopt strategies that work in harmony with our body's intrinsic design, paving the way for long-term wellness.

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Key Words:

Pandemic:
a widespread outbreak of an infectious disease that affects large populations across countries or continents, often causing significant health, social, and economic disruption

Immunity:
the body's ability to resist or fight off infections and diseases

TRINITY 2025

Not If, But When: Emerging Infections and the Future of Health

By Juhi Bhatia (Year 11)

In 2020, the world came to a standstill. Economies slowed, toilet paper shelves emptied, and millions of lives were disrupted by a single emerging infection: COVID-19. Experts now warn there is a '50% chance of another pandemic within the next 25 years.' (Kerry and Basu, 2025) The question we face is simple: are we truly prepared, or will the next crisis send us tumbling?

Lasting impacts from our most Recent Pandemic, COVID-19

Lockdown became the most visible scar of COVID-19. Loneliness turned into an epidemic of its own, as simple pleasures: chatting with a friend or going for a walk, suddenly carried rules and restrictions if you weren't in the same 'bubble.' At the third level of Maslow's Hierarchy of Needs sits love and belonging, a fundamental human need that lockdown ruthlessly stripped away. It's no wonder The World Health Organization (2022) reported that 'in the first year of the COVID-19 pandemic, global prevalence of anxiety and depression increased by a massive 25%.'

Not only this, but lockdowns such as these have lasting impacts on learning. Education shapes our future. The lessons we acquire today become the skills we carry into tomorrow. Yet the pandemic brought learning to a halt. Students attended classes from their beds, cameras turned off, distractions at hand. Months became years, and upon returning to school, many struggled with the basics- some even forgot how to hold a pen. Studies confirm this setback. Research by the University of Oxford (2023) revealed that pupils lost nearly a third of their expected learning during the pandemic. The consequences of this loss stretch far into the future: weaker foundations mean lasting gaps in knowledge, and for some, opportunities were cut short altogether. Many students never even sat their GCSEs or A-levels; instead, grades were predicted by teachers, leaving many feeling robbed of a chance to prove themselves.

Global Inequalities in Emerging Infections

Those who are privileged enough to live in an economically stable country suffer less from emerging infections, as they have the resources to combat them. Others are not so lucky. In Sub-Saharan Africa, fragile healthcare systems make the region more vulnerable to emerging infections. Over 70% of the world's HIV/AIDS cases are concentrated in Sub-Saharan Africa, leaving millions with weakened immunity and at higher risk from diseases such as tuberculosis, which alone claims more than 400,000 lives annually in the region (Joshi et al., 2021).

Limited resources mean these healthcare systems

Key Words:

Emerging Infection:
an infectious disease that has recently appeared in a population or is rapidly increasing in incidence or geographic range, often due to changes in environment, human behaviour, or microbial evolution

Transmission:
the process by which a disease, signal, or substance is passed from one person, organism, or place to another, often through direct contact, air, fluids, or vectors like insects

struggle to meet demand. In 2009, low-income countries spent an average of just 6.1% of GDP on health, compared with 9.5% in wealthier OECD nations (World Health Organization, 2010). Yet in absolute terms, this represents far fewer doctors, hospital beds, and medical supplies. The arrival of a new pandemic would quickly overwhelm such fragile systems. In these contexts, emerging infections are not a temporary disruption but a permanent crisis, a reminder that pandemics rarely strike all countries equally.

Will there be Another Lockdown?

If previous pandemics have taught us anything, it is that lockdowns come at an eye-watering economic cost. Shops shuttered, businesses collapsed, and entire industries ground to a halt. In the years that followed, inflation spiralled: in 2020, UK consumer prices were relatively low, but by June 2022, the Consumer Prices Index including owner occupiers' housing costs (CPIH) had risen to 8.2%. For many households, that meant one thing: less money in their pockets. Essentials like fresh food, heating, and even basic medicines suddenly felt like luxuries. And while the most vulnerable struggled to make ends meet, rising healthcare costs placed treatment further out of reach. What happens when conditions go untreated? Poorer health. More stress. For some, an escape through addiction, as the National Institute on Drug Abuse (2020) reveals, '13% of Americans have reported increasing or starting substance use as a way of coping with stress related to the pandemic.'

Governments know this. They know that another nationwide lockdown would be unaffordable, unfair on many of the working class and create a deeper divide between rich and poor. We cannot afford to gamble with our economies or our well-being in the same way again.

Approaching an Emerging Infection

Emerging infections rarely arrive with warning. One day, it is a handful of cases; the next, it is a crisis. So, what can *you* do to help prevent a global pandemic? Small actions matter. Wash your hands regularly, practise good hygiene, and stay home when unwell; these are simple steps that cut transmission. Stay informed. Following trusted advice rather than rumours protects not only you, but everyone around you. Because the truth is, emerging infections are inevitable, but it is on *us* as a society to reduce the chances of history repeating itself.

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TRINITY 2025

Does Brain Size Correlate with Intelligence in Humans?

By Imaani Ahmed (Year 13)

Key Words:

Neuroscience: the scientific study of the nervous system, including the brain, spinal cord, and neural networks, aiming to understand how they control behaviour, cognition, and bodily functions

Neurones: specialised cells in the nervous system that transmit electrical and chemical signals to and from the brain, spinal cord, and other parts of the body, enabling communication, sensation, and movement

Intelligence is a complex and multifaceted trait encompassing problem-solving, memory, reasoning, creativity, and adaptability. Since the 19th century, researchers have debated whether brain size plays a crucial role in determining intelligence. Early theories proposed a direct relationship between brain volume and cognitive ability, suggesting that individuals with larger brains possess superior intelligence. However, modern neuroscience has revealed a more nuanced understanding; incorporating neural density, connectivity, and environmental factors as critical determinants of intelligence.

This essay critically examines the extent to which brain size correlates with intelligence in humans. It explores historical perspectives, modern neuroscientific findings, and counterarguments that challenge the brain-size hypothesis. Additionally, it evaluates alternative predictors of intelligence, including neuron density, cortical organization, and white matter efficiency. By integrating multiple perspectives, this analysis aims to determine whether brain size is causally linked to intelligence or if other factors play a more significant role.

What is Intelligence and how is it Linked to the Brain?

Intelligence can be difficult to define; the ability to acquire and apply knowledge, the capacity to process and manipulate information, an adaptive trait that allows organisms to survive and thrive in their environments learning from past experiences - there are multiple aspects to intelligence, therefore there isn't a single universally accepted definition. This could be due to the existence of different types of intelligence, including emotional, general, social, creative, practical, spatial, and logical - there are many different ways to measure intelligence and therefore different areas of the brain are responsible for a wide range of functions, each relating to unique aspects of intelligence.

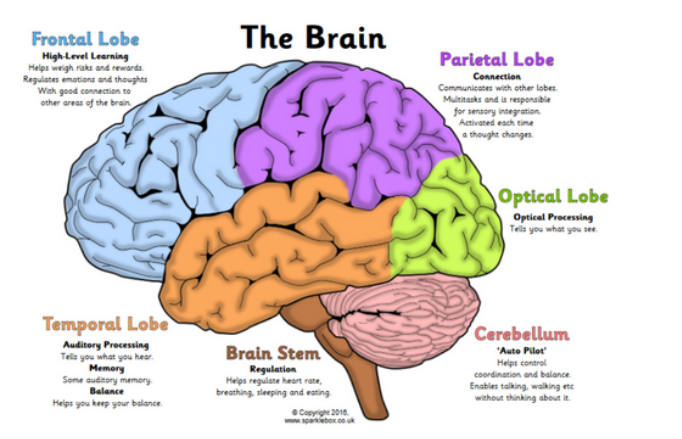

Figure 1. Lobes of brain and control (SparkleBox, 2018)

Intelligence is intrinsically connected to neurons, the specialized cells that process and transmit information through electrical and chemical signals, creating a vast and intricate web in the brain. The brain consists of approximately 86

billion neurons! Did you know that, depending on the size of the myelinated axons in the neurons, neurons can transmit signals at around 268 miles per hour? The number of neurons in a specific brain region affects cognitive ability; for example, humans have a much higher concentration of neurons in the brain compared to other species, which contributes to advanced cognitive abilities (we have a high neuron density in the cerebral cortex, responsible for decision-making, abstract reasoning and complex thought processes). However, intelligence is not just about the density of neurons, but also how well they are connected. The strength and efficiency of synaptic connections determine how effectively different brain regions communicate, and therefore how fast information can be retrieved/processed. This correlates to intelligence and one's intellectual aptitude because stronger, faster, and better-connected neurons enable the brain to handle information more efficiently and accurately.

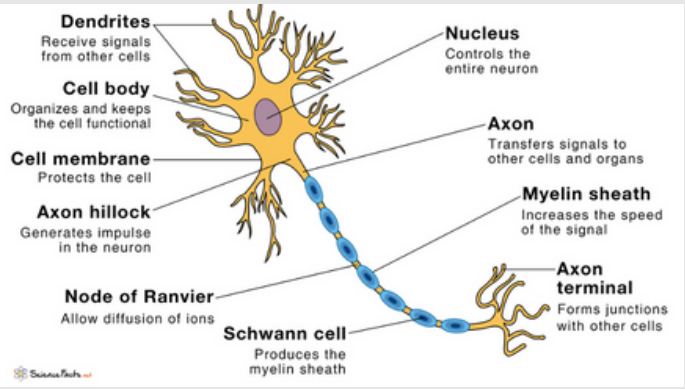

Figure 2. Parts of a neuron with functions (ScienceFacts, n.d.)

Brain Size and Intelligence: The Traditional/Conservative View

The idea that larger brains indicate higher intelligence has historical roots in the works of early scientists such as Paul Broca and Samuel Morton. Broca (1861) measured cranial capacity (the volume of the skull that holds the brain) and concluded that brain size correlated with intelligence, while Morton (1849) used skull measurements to support racial hierarchies in intelligence—claims that were later discredited due to methodological biases, and proved scientifically invalid. Despite these historical misinterpretations, the question of brain size as a predictor of intelligence has persisted into modern research.

Several contemporary studies have reported a modest positive correlation between brain volume and intelligence. McDaniel (2005) conducted a meta-analysis of MRI studies and found a correlation of approximately 0.33–0.4 between total brain volume and IQ scores, indicating a moderate positive relationship between total brain volume and IQ scores. In other words, people with larger brain volumes tended to have slightly higher IQ scores, but the relationship is not very strong (as correlation ranges from -1 to +1, where 1 is a perfect positive correlation). Similarly, Rushton and Ankney (2009) found that individuals with larger brains tended to score higher on standardized intelligence tests. These findings suggest that brain size may have some influence on cognitive function, but the relationship remains relatively weak and inconsistent across studies. This leads scientists to believe this isn't the only determining factor of intelligence and the correlation does not necessarily imply a causal relationship.

Counterargument: Brain Size Alone is an Incomplete Measure

Despite evidence suggesting a potential correlation, many neuroscientists argue that brain size alone is insufficient to determine intelligence. One major criticism is that individual intelligence can vary greatly, even among people with similar brain volumes. Deary et al. (2010) found that while some highly intelligent individuals had large brains, others with comparable IQs had average or even below-average brain volumes. This inconsistency challenges the assumption that size directly decides intelligence.

A key example is the case of Albert Einstein,

whose brain was slightly smaller than average (~1230 cm^3< 1400 cm – Einstein < average), yet he exhibited extraordinary cognitive abilities. Post-mortem analysis revealed that Einstein's brain had a uniquely developed prefrontal cortex, increased glial cell density, and a high number of inter-neuronal connections (Witelson et al., 1999). An increased glial cell density shows that Einstein had more 'supportive' cells in his brain as glial cells are responsible for maintaining brain health and protecting neurons. A high number of inter-neuronal connections could perhaps relate to enhanced communication between neurons, enabling faster and more transmission of signals. This extraordinary case study suggests that intelligence may depend more on neural efficiency and brain organization rather than sheer size.

Furthermore, sex differences in brain volume undermine the brain-size hypothesis. On average, male brains are approximately 10% larger than female brains (Haier et al., 2005), yet intelligence tests show no significant differences in cognitive abilities between sexes (~1200 cm3 < ~1400 cm3 – female < male). This discrepancy highlights the importance of structural and functional differences rather than absolute brain size.

Neural Density, Structure, and Connectivity: A More Accurate Predictor?

A growing collection of research suggests that intelligence is more closely linked to neuron density (number of neurons per unit of brain tissue), cortical organization (how neurons are arranged and structured in the cortex), and brain connectivity (the network of neural connections) rather than overall volume.

Herculano-Houzel (2009) proposed that the number of neurons, particularly in the cerebral cortex, is a better predictor of cognitive ability than total brain size. While elephants and whales have larger brains than humans, their neuron density is significantly lower. In contrast, the human brain, despite being smaller, contains approximately 86 billion neurons, with a disproportionately high concentration in the prefrontal cortex, which governs reasoning, planning, and problem-solving. Thus suggesting that brain size doesn't determine intelligence, but perhaps the density of neurons as it plays a crucial role in allowing humans to out-perform other larger-brained species cognitively.

Key Words:

Synapse:
the junction between two neurones where signals are transmitted, either chemically via neurotransmitters or electrically

Meta-analysis:
a statistical method that combines results from multiple independent studies on the same topic to identify overall trends, increase reliability, and draw stronger conclusions than any single study alone

Neuroplasticity:
the brain's ability to reorganise and form new neural connections throughout life, allowing it to adapt to learning, experience, injury, or changes in environment

The prefrontal cortex is known as the brain's control centre for sophisticated cognitive processes. Studies have shown that individuals with greater cortical surface area and higher prefrontal activity tend to exhibit better performance on intelligence tests (Jung & Haier, 2007). Moreover, increased activity in the prefrontal region has been linked to higher IQ scores. This indicates that the efficiency of information processing in specific brain regions is more relevant to intelligence than absolute brain size.

In addition, recent findings emphasize the importance of white matter and neural connectivity in determining intelligence. White matter refers to the tissue in the brain that

contains the long-range nerve fibres (axons) wrapped in myelin, which helps in transmitting electrical signals between different regions of the brain - the brain's communication network. Colom et al. (2006) found that individuals with higher IQs exhibited stronger white matter integrity, which enhances the speed and efficiency of neural communication. Similarly, Barbey et al. (2012) demonstrated that intelligence is not limited to a single brain region but is instead distributed across networks that integrate multiple cognitive functions in multiple brain regions, that are all interconnected.

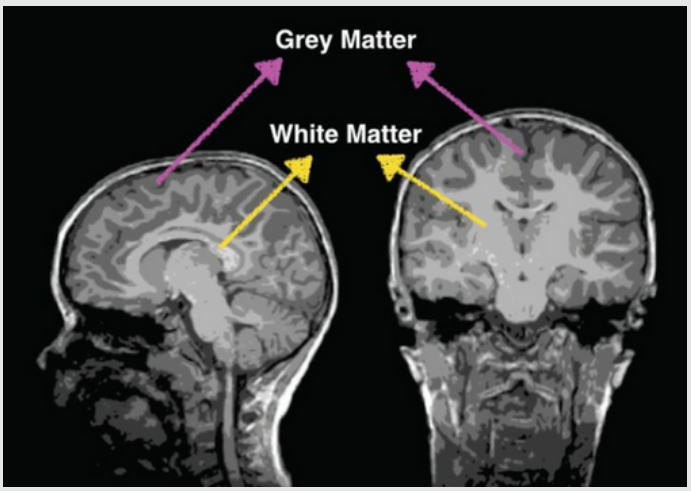

Figure 3. (Ansari, 2008)

While biological factors play a fundamental role in intelligence, environmental influences also contribute significantly.

Twin studies suggest that intelligence is highly heritable, with approximately 50-80% of its variation due to genetic factors (Plomin & Deary, 2015). These studies compare the similarity in intelligence between identical twins (share 100% of their DNA) and fraternal twins (share 50% of their DNA). This illustrates the importance of genes in shaping cognitive abilities. However, specific genes associated with brain size, such as ASPM and MCPH1, do not show a direct link to intelligence (Montgomery et al., 2011). This suggests that intelligence is polygenic and influenced by complex genetic interactions rather than a single determinant like brain size.

Environmental Factors and Neuroplasticity

Environmental factors such as nutrition, education, and social stimulation shape cognitive abilities. Neuroplasticity, which refers to the brain's ability to reorganize itself by forming new neural connections in response to new learning and experience, plays a crucial role in intelligence development. Nisbett et al. (2012) found that early childhood interventions, including cognitive enrichment and quality education, significantly enhance IQ levels by stimulating neuroplasticity, thereby improving cognitive function. These environmental factors help to positively stimulate neuroplasticity by encouraging new learning experiences, achieving emotional regulation and by engaging in cognitive challenges. By supporting these factors, the brain's ability to adapt and grow can be enhanced, ultimately improving cognitive abilities.

Conclusion

The correlation between brain size and intelligence in humans is complex and remains an interesting topic of ongoing research. While some studies suggest a modest positive relationship, there is insufficient evidence to establish a causal link between brain volume and intelligence. The unreliable association, coupled with counterexamples such as Einstein's brain and sex differences in brain size, indicate that intelligence is not simply a function of brain size.

Instead, intelligence is better explained by factors such as neuron density, cortical structure, brain connectivity, and environmental influences. Rather than viewing intelligence as a direct function of brain size, modern neuroscience supports a more refined and holistic perspective, emphasizing brain efficiency, adaptability, and plasticity. Future research should further investigate the various neural mechanisms that contribute to intelligence and explore how genetic and environmental factors interact to influence cognitive potential.

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Key Words:

Alzheimer's
a brain disease that gradually destroys memory and thinking, leading to confusion and loss of independence

Epilepsy:
a neurological disorder marked by recurrent seizures due to abnormal electrical activity in the brain

Hippocampus:
a brain region crucial for memory formation, learning, and spatial navigation

Cutting-Edge Brain-Computer Interface Research in Alzheimer's Disease

By Cunyi George Xu (Year 13)

What is Brain-Computer Interface and why does it Matter for Alzheimer's Disease?

A brain-computer interface (BCI) is technology that can read brain signals and translate them into commands for external devices, or write signals back into the brain through targeted stimulation.

For Alzheimer's disease (AD), brain-computer interfaces (BCIs) could revolutionize care by enabling early detection through the identification of abnormal brain rhythms before symptoms become apparent, supporting communication by allowing patients with speech difficulties to express basic needs, and offering therapeutic intervention via targeted brain stimulation to reinforce memory networks or enhance the brain's natural "waste clearance" processes.

Seeing Memory Networks: Closed-Loop Stimulation and Memory Prostheses

In epilepsy patients undergoing intracranial monitoring, researchers have shown that precise, timed stimulation of the hippocampal-temporal network during "plasticity windows" can improve memory recall (Ezzyat et al., 2018).

The principle behind the "memory prosthesis" involves decoding an individual's brain activity during memory encoding and then replaying or enhancing those patterns during recall. Although this technique has not yet been widely tested in Alzheimer's disease (AD), its relevance is underscored by the fact that the hippocampus—central to memory formation—is among the earliest regions affected in AD (Hampson et al., 2018; Hampson et al., 2021).

Deep Brain Stimulation (DBS) in the Fornix

Another more invasive "write" approach is deep brain stimulation (DBS). Trials targeting the fornix —a key memory pathway—have produced mixed results: no consistent clinical benefit overall, but signs of metabolic and cognitive improvement in certain subgroups (Lozano et al., 2016). This suggests that future AD DBS may require patient stratification, personalised stimulation parameters, and combination with drugs or rehabilitation.

Non-Invasive Rhythm Stimulation: The 40 Hz Clean-Up Beat

The brain's gamma rhythm (~40 Hz) appears to help microglia—the brain's immune cells—clear

Key Words:

Neurofeedback:
a technique that trains individuals to regulate brain activity by providing real-time feedback from EEG signals

Vascular:
relating to blood vessels, which carry blood throughout the body and support circulation and tissue health

Cognitive:
relating to mental processes like thinking, learning, memory, and decision-making

toxic proteins. In mice, 40 Hz light and sound stimulation reduces amyloid-beta deposits and improves memory (Martorell et al., 2019). Early human studies show safety and preliminary biomarker changes (e.g. slower brain atrophy), though larger trials are needed to confirm cognitive benefits. The appeal: wearable, at-home devices delivering sensory stimulation as part of a lifestyle-based therapy.

EEG Neurofeedback and Home-Based Light BCI

Neurofeedback—real-time visualisation of brain rhythms with training to modulate them—has shown short-term improvements in working memory and attention in mild cognitive impairment (MCI) and mild AD (Holczer et al., 2020). This low-risk approach can be combined with cognitive training, forming a multi-modal brain fitness programme at home.

Early Screening: from Reading to Risk Spotting

BCI's "read" capability is also being used for risk identification. In simple EEG tasks (viewing images, hearing words), event-related potentials (ERP) and phase synchrony can detect subtle memory-processing abnormalities. Combined with AI, this could pre-select individuals for confirmatory AD tests (e.g. plasma p-tau217, PET).

Challenges Ahead

Key challenges for brain-computer interface (BCI) applications in Alzheimer's disease include ensuring consistency and durability, as most findings currently stem from small, specific cohorts and require validation through larger randomised trials; achieving personalisation by determining the optimal frequency, intensity, and neural targets for each patient at different stages of disease; integrating BCIs with pharmacological treatments such as anti-amyloid antibodies, alongside vascular risk management and lifestyle interventions; and addressing accessibility and ethical concerns, particularly as non-invasive devices offer scalability but must be matched by robust approaches to data privacy, user adherence, and sustainable funding models.

Practical Takeaway

For families, engaging in non-invasive gamma stimulation or neurofeedback combined with cognitive training is generally considered low risk and can serve as a valuable complement to healthy lifestyle practices. Foundational habits like maintaining good sleep, regular exercise, and controlling blood pressure and glucose levels remain essential for brain health. When exploring BCI technologies, it's important to select devices backed by clinical trials or endorsed by reputable medical institutions, while consistently monitoring cognitive performance and daily functioning over time.

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TRINITY 2025

De-Extinction? A Deep Dive into Restoration and DNA

By Nikhil Chunduri (Year 11)

Key Words:

De-extinction:
the process of reviving extinct species using genetic engineering, cloning, or selective breeding techniques

Back-breeding:
a selective breeding method that aims to recreate traits of an extinct ancestor by mating its closest living relatives over generations

Cloning:
creating a genetically identical copy of an organism, cell, or DNA sequence

Introduction

The concept of de-extinction—reviving extinct species—has transitioned from science fiction to scientific possibility. With recent developments such as the attempted resurrection of the dire wolf, the feasibility of reintroducing extinct organisms has garnered increasing attention (Ord, n.d.). This raises critical questions about the mechanisms behind such efforts. Do scientists extract DNA from fossils? What technologies make this possible? Currently, three primary methodologies underpin de-extinction research: back-breeding, cloning, and genome editing.

Back-Breeding

Back-breeding is a selective breeding technique aimed at reintroducing ancestral traits that have been lost or diluted in modern descendants. The objective is either to restore a species' original phenotype or to reinforce specific genetic characteristics (Ord, n.d.). Although considered more natural than other methods, back-breeding is constrained by its lengthy timescale and environmental mismatches between ancestral and modern ecosystems. For instance, atmospheric composition and hydrological conditions have changed significantly, potentially affecting the viability of reintroduced traits.

A notable example is the "Iron Age pig" project, which sought to recreate the phenotype of the European wild boar by crossbreeding wild boars with Tamworth pigs—a British domestic breed. While some farmers, such as Oskar Ohlson, report that these hybrids are docile and stress-reactive (Wikipedia, 2024a), others observe more aggressive behaviours, likely due to the genetic variability between the parent breeds (Wikipedia, 2019). This highlights the unpredictability of temperament and phenotype in back-bred hybrids.

Cloning

Cloning involves the creation of genetically identical organisms and is categorised into gene cloning, therapeutic cloning, and reproductive cloning. Gene cloning replicates specific DNA sequences, therapeutic cloning generates embryonic stem cells for research, and reproductive cloning produces entire organisms (National Human Genome Research Institute, 2020). However, cloning requires intact living cells, rendering it unsuitable for species that are entirely extinct.

Despite this limitation, cloning remains valuable for bolstering endangered populations. For example, the Pyrenean ibex (Celia), which became extinct after a tree accident, was cryopreserved and later cloned using nuclear transfer—a process involving

the transplantation of a donor nucleus into an enucleated egg cell. Although the cloned ibex died shortly after birth due to a lung defect, the attempt marked the first successful cloning of an extinct subspecies (Wikipedia, 2024b).

Genome Editing

Genome editing enables precise modifications to DNA sequences through insertion, deletion, or replacement at targeted loci. This process typically begins with the induction of a double-stranded break (DSB) in the DNA, often facilitated by restriction enzymes. However, traditional enzymes lack site-specific precision, prompting the development of engineered nucleases such as mega-nucleases, zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and CRISPR-Cas systems (Wikipedia, 2022).

CRISPR-Cas9

CRISPR-Cas9 is a naturally occurring bacterial defence mechanism adapted for genome editing. CRISPR sequences store fragments of viral DNA, while Cas9 enzymes use RNA guides to identify and cleave matching sequences during subsequent infections (TED-Ed, 2017). In biotechnology, scientists design guide RNAs to target specific genes, enabling Cas9 to perform precise cuts and facilitate gene editing.

Zinc-Finger Nucleases

Zinc-finger proteins bind to specific three-nucleotide sequences within DNA, functioning as molecular GPS units. Upon locating their target, they recruit co-repressors via the KRAB domain to silence or activate genes (Wikipedia, 2017). When fused with the restriction enzyme FokI, which contains a nuclease domain, two ZFNs can bind to adjacent DNA sequences and induce a DSB (Wikipedia, 2024c).

TALENs

TALENs, derived from plant-pathogenic bacteria, operate similarly to ZFNs. They consist of DNA-binding domains fused with FokI nucleases. Once engineered into plasmids and introduced into cells, TALENs induce DSBs, allowing for gene deletion or alteration (Lucas Learns, 2022). Although effective, TALENs have largely been superseded by CRISPR-Cas9 due to its simplicity and efficiency.

Key Words:

Genome Editing:
a technique that alters DNA sequences within an organism's genome to modify traits or correct mutations

Nuclease:
an enzyme that cuts DNA or RNA strands by breaking the bonds between nucleotides

Mega-Nucleases

Mega-nucleases are capable of targeting up to 40 base pairs within double-stranded DNA, offering high specificity. They can either silence genes by targeting exons or insert new genes by modifying introns (Wikipedia, 2010). Understanding the distinction between exons and introns is essential: exons are coding regions retained during mRNA splicing, while introns are non-coding segments removed during transcription (Wikipedia, 2023a; Wikipedia, 2023b).

Conclusion

De-extinction is no longer a speculative concept but a tangible scientific pursuit. Techniques such as cloning and CRISPR-Cas9 have demonstrated the potential to revive extinct species or reinforce dwindling populations. While DNA degradation remains a significant challenge, advances in genome engineering suggest that even ancient species—perhaps dinosaurs—could one day be reconstructed using the genetic material of their modern relatives. As technology progresses, the boundaries between extinction and existence may continue to blur, offering profound implications for biodiversity and conservation.

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Key Words:

Huntington's: a genetic brain disorder causing progressive movement, cognitive, and psychiatric decline due to nerve cell damage in specific brain regions

Huntington's: a protein produced by the HTT gene, essential for normal brain development but mutated in Huntington's disease

TRINITY 2025

Huntington's Disease: Editing the Future, Living the Present

By Bahara Qalandari (Year 13)

Everyone has the odd broken watch lying around that your mum insists to 'fix one day'. It makes you wonder: how did the watch break in the first place? Most of the time, one small gear breaks, but the watch still ticks. Over time that broken piece wears on the other parts, and slowly the whole watch stops working.

Huntington's disease works in a similar way: a single faulty gene is like the broken gear. At first things may seem normal, but as time goes on, the minor, unnoticeable error disrupts movement, thinking and emotions (Health Direct, 2023).

Huntington's disease (HD) is a progressive, inherited neurodegenerative disorder that causes the gradual breakdown of brain cells, leading to problems with movement, behaviour and cognition. It is named after physician George Huntington, who first described the disease in 1872 (Medline Plus, 2020).

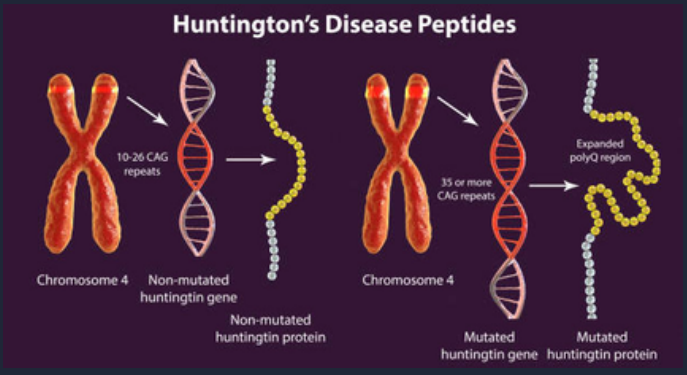

Figure 1. (Mental Matters, n.d.)

Huntington's disease is caused by a mutation in the HTT gene on chromosome 4. This gene is responsible for making a protein called huntingtin. The mutation involves a DNA sequence —CAG (which codes for the amino acid glutamine)—being repeated too many times (Caron, Wright and Hayden, 2018).

The mutated huntingtin protein is toxic to brain cells, especially in areas like the basal ganglia (which controls movement) and the cortex (responsible for thought and emotion). Over time, this leads to brain atrophy, or shrinkage (National Institute of Neurological Disorders and Stroke, 2025; Tabrizi et al., 2019).

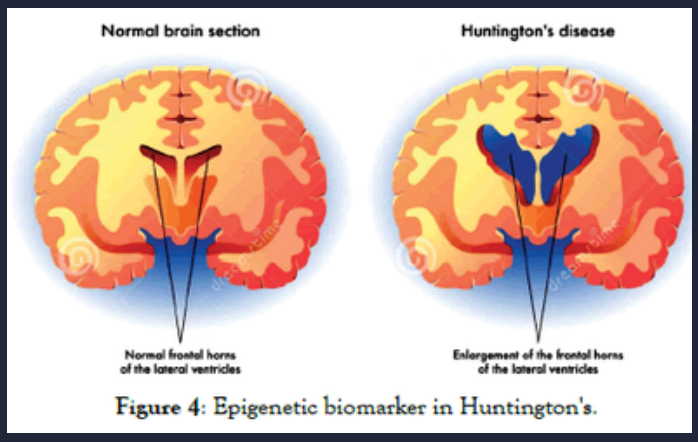

Figure 2. (Smith et al., 2011)

Huntington's disease is passed from parent to child in an autosomal (disease affects both males and females equally), dominant (only one copy of the altered gene from either parent is enough to

Key Words:

Chorea:
involuntary, rapid, and unpredictable movements, often affecting the face, hands, or feet

Predictive Testing:
a genetic test used to determine the likelihood of developing a hereditary disease before symptoms appear

cause the disease) pattern. This means a child has a 50% chance of inheriting the disease if one parent has it, which will eventually develop the disease (Medline Plus, 2020). There is currently no cure, but treatments can help manage symptoms and improve quality of life (Stoker et al., 2022).

Symptoms usually begin between the ages of 30 and 50, though they can appear earlier or later. Common signs include chorea (involuntary movements), mood changes (like depression or irritability), and difficulty with memory and decision-making. Over time, these symptoms worsen, leading to significant disability (Health Direct, 2023; Caron, Wright and Hayden, 2018).

Woody Guthrie, the iconic American folk musician and songwriter, was diagnosed with Huntington's disease later in his life. Although the disease was not well understood at the time, Guthrie began showing symptoms in the late 1940s and early 1950s. His symptoms gradually worsened, seriously impacting his ability to perform, write music, and maintain his career. Eventually, Guthrie was hospitalised for many years due to the progression of HD, which forced him into early retirement from music. Despite his decline, Guthrie's legacy lived on through his influential songs and his family, including his son Arlo Guthrie, who continued the musical tradition. His struggle with Huntington's also helped raise awareness about the disease, which was little known at the time (National Institute of Neurological Disorders and Stroke, 2025).

Some families can take voluntary predictive testing (especially for families with a history of HD) but struggle making the decision, knowing it can bring relief or increase worries. The 50% risk of inheriting the mutated gene creates lifelong anxiety for children of affected parents (Medline Plus, 2020). Many never find out, as their family consider their symptoms as 'just getting older' (Health Direct, 2023).

Even families who do know are under an overwhelming amount of stress. Family members frequently take on the role of primary caregivers, especially as the disease progresses. Caregivers often face physical exhaustion, emotional burnout, social isolation and financial stress (Stoker et al., 2022).

Additionally, families often experience anticipatory grief — mourning the loss of a loved one's personality, abilities, and independence long before physical death. Some experience complicated grief, especially if the disease causes dramatic personality changes, aggression, or cognitive decline (Caron, Wright and Hayden, 2018).

There is often a lack of public understanding about HD. Families may feel isolated or ashamed, especially if behavioural symptoms (e.g. aggression, psychosis) are misinterpreted by others. HD is sometimes called a "family secret" as relatives may hide diagnoses due to stigma or fear of discrimination (e.g. in employment or insurance) (National Institute of Neurological Disorders and Stroke, 2025).

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TRINITY 2025

The Brain's Fire Alarm: Exploring Cluster Headaches

Key Words:

Migraine: a neurological condition causing intense headaches, often with nausea, light sensitivity, and visual disturbances

Trigeminovascular: relating to the interaction between the trigeminal nerve and brain blood vessels, key in migraine pain pathways and inflammation

By Hiba Mohamed Hamzath (Year 13)

Cluster headaches, also nicknamed 'suicide headaches' due to their intensity and unbearable pain, involve excruciating head pain, with a burning, stabbing sensation behind one eye, and are often described as the most painful type of headache known to medicine. Cluster headaches get their name from how they affect you, so unlike, migraines or tension headaches, cluster headaches strike in 'bouts' or clusters, often at the same time each day or during certain seasons, and this has led scientists to link them to the body's internal clock. However, while cluster headaches are extremely disabling, they also remain one of the biggest mysteries in neuroscience - and scientists are still working to unlock the truth behind them. In many ways, cluster headaches act like a fire alarm in the brain — a sudden, overwhelming warning signal that disrupts daily life, yet one whose underlying cause remains elusive.

What are Cluster Headaches?

Cluster headaches are another form of headaches that are categorized by cyclical patterns or pains. Contrasting to migraines, which tent to come much slower, the cluster headache strikes quickly. (Global Nerve Foundation, 2022) Symptoms usually include sudden pain, normally around one eye, with pain reaching its highest within 10-15 minutes. It also includes eyelid drooping/swelling, red or watery eyes and changes in the pupil of the eye (John Hopkins Medicine, n.d). During an active cycle, individuals can experience up to 8 attacks a day. These 'attack cycles' can last up to 6 - 12 weeks, with remissions lasting up to a year. They are quite rare, only affecting around 1 in 1000 individuals (0.1% of population), and it has been discovered that men are more likely to suffer from these headaches compared to women, more specifically those in their 30s-40s. Many of those who have cluster headaches have a personal or family history of migraines (Mount Sinai, 2020).

The Science Behind Cluster Headaches

Though researchers are unaware of the full causes of cluster headaches, it has been found to link to the sudden release of histamine or serotonin. The use of alcohol, smoking cigarettes, change to a high altitude, bright light, exercise, cocaine use and foods that contain nitrates e.g. bacon, have all been linked to triggering these headaches (John Hopkins Medicine, n.d). Due to the periodicity of these headaches, investigations were done in the hypothalamus, the part of the brain which controls our body clock, and this led them to find some unusual differences in its structure when looking at it through morphology studies. There have also been findings of potential involvement of the trigeminovascular system and parasympathetic nerve fibres, however the manner

in which these structures interact to cause these headaches is not definite. This has led some researchers to liken cluster headaches to a misfiring brain fire alarm, where the hypothalamus and nervous system pathways overreact, sounding a signal of intense pain without a clear or proportional trigger. Furthermore, as there is a certain familial connection, a significant effort has gone into analysing the genetics of the condition (Kandel & Mandiga, 2023). This led to the realisation that genetic factors do contribute to cluster headaches but are only part of the picture.

Treatments and Coping

For these types of headaches, there are 2 types of treatments, the first one being acute treatments. The goal of acute treatments is to stop/relieve the headache once it has started. 6mg injections of Sumatriptan provides relief remains the most effective pharmacological option, and is supposed to provide relief within 15 minutes. High-flow oxygen therapy (100% oxygen at 7-15 L/min for 15-20 mins) is also an effective way of stopping these attacks. For individuals who cannot tolerate such approaches or for those who find them insufficient, intranasal triptans, such as sumatriptan or zolmitripan, can be used. In addition to this, non-invasive vagus nerve stimulation with a gammaCore device has shown efficacy both as an acute and preventative treatment option, which means that the frequency, severity and duration of the attacks may be reduced using this. Further preventative care treatments could be Verapamil, which remains the first-line preventative agent. However, due to its potential to cause abnormal cardiac rhythms, regular ECG monitoring is required. Additional options include greater occipital nerve block (GON), which involves targeted injection at the optical nerve and demonstrates an average efficiency of almost 50%. Corticosteroids may also provide rapid, short-term benefit, thought their use is limited by side effects and unsuitability for long-term therapy. Other preventative measures with evidence of effectiveness includes lithium, melatonin supplementation and sphenopalatine ganglion stimulation. In terms of lifestyle, patients are also advised to avoid recognised triggers during active cluster periods (The Migraine Trust, 2021). Cluster headache sufferers are also recommended to stick to a regular sleep schedule, as changes in sleep schedule can trigger headaches, especially during these cluster periods (Mayo Clinic Staff, 2025).

Key Words:

ECG (Electrocardiogram):
a test that records the heart's electrical activity to detect rhythm abnormalities, heart damage, or other cardiac conditions

Corticosteroids:
a class of steroid hormones that reduce inflammation and suppress the immune system

Conclusion

Cluster headaches stand out not only as one of the most painful conditions known in medicine, but also as one of the most perplexing. Despite advances in identifying triggers, neural pathways, and effective treatments, the full picture of why these headaches occur remains incomplete. Their cyclical timing, genetic links, and response to both pharmacological and lifestyle interventions highlight how complex they are, with branches in neurology, genetics, and chronobiology. Much like a fire alarm that rings without an obvious fire, cluster headaches continue to warn us of underlying processes that science has yet to fully decode. Until those mysteries are solved, treatments will remain focused on managing attacks and reducing suffering, while researchers strive to uncover the deeper systems behind the brain's most agonising alarm.

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