Morphine's journey through the body: mechanisms behind opioid pain relief

Kira Sidhu (Spain)

The Biochemical Society identifies and celebrates outstanding science communication talent in molecular biosciences with its annual Science Communication Prize. Kira Sidhu, from Spain, won the third prize in the written category for students studying for A-level/T-level/BTEC National/Scottish Highers or equivalent qualifications. Kira's piece is titled 'Morphine's journey through the body: mechanisms behind opioid pain relief'.

Introduction from the author

Morphine is a strong opioid drug that has been used by mankind for centuries, most commonly for pain relief purposes. Known for its anesthetic and euphoric abilities, morphine, along with other opioids, is frequently given in medical settings to quickly and effectively eliminate sensations of pain. But what specifically does it do to accomplish this? After entering your system, how is morphine able to silence messages of pain in and around the nervous system? And in a world where opioid addiction has reached epidemic levels in many countries, affecting millions of lives, what can its effect on the body tell us about preventing dependence upon it?

This article seeks to answer these questions by investigating the journey of a dose of morphine through the body and how sensations of pain relief and other effects are caused in this manner.

Morphine's journey through the body: mechanisms behind opioid pain relief

Morphine was given its name from that of the Greek god of dreams, but 'dreams' don't seem to come close to describing its otherworldly effect. Classified as an opioid, morphine is known for its analgesic, or extreme pain-eradicating, properties, giving it a merciful effect on those suffering from agonizing injuries or ailments (Figure 1).

From the perspective of an individual using this potent opioid, we will follow the injected dose of morphine as it travels through the bloodstream and brain to understand the dramatic and dynamic effects it has on the human body.

Gripping the barrel of the syringe, you carefully guide the needle into place under the soft skin on the inside of your elbow. In a singular motion, you press down on the plunger, pushing the liquid morphine into your vein and setting it free into your bloodstream.

The morphine travels within your veins, spreading to different areas of the body. Once the drug travels through the blood up to the area around the brain, it has to cross the blood–brain barrier to make its way into the brain tissue. Since this barrier is quite hydrophobic ('water fearing') while morphine is hydrophilic and not particularly lipid-soluble, this can take a longer time to happen relative to more lipophilic drugs such as fentanyl.[1]

Once inside brain tissue, it begins to take effect on the central nervous system – the part of the nervous system involved in processing, including the processing of pain signals – which exists as a network of neurons within the brain and the spinal cord.

Neurons communicate with each other using neurotransmitters, which are the chemical messengers released by a neuron (which we will call the presynaptic neuron) whose messages are transferred back into electrical signals once they are received by the next neuron (called the postsynaptic neuron) (Figure 2).

Within the brain, morphine binds strongly to opioid receptors found on neuronal cell membranes in neurons responsible for pain-signaling. Binding to opioid receptors at the presynaptic nerve terminal works to prevent neurotransmitters from being released. Essentially, the message that pain is being sensed at a specific location in the body is prevented from being communicated.

This means that in the postsynaptic (signal-receiving) neuron, morphine is having an inhibitory

Figure 1. Morphine. October 2022. United States Drug Enforcement Administration, https://www.dea.gov/factsheets/morphine. Website: https://www.dea.gov/factsheets/morphine

effect; the activity of this neuron is decreased since the pain signal could not be sent via neurotransmitter.[2]

Very quickly, a merciful relief begins to set in. The throbbing pain you felt just moments ago has died away. And within the first 20 minutes, a blissful euphoria envelops you as the drug works at its peak performance within you.

The binding of morphine to opioid receptors also causes the release of dopamine, a neurotransmitter known to be connected to pleasure, in the brain.

Overall, the net effect of morphine prevents the user from experiencing sensations of pain – and for a significant period of time as well. Morphine will generally continue to relieve pain for up to 4–6 hours after being taken. Its long-lasting effects can be attributed to a few factors, including the blood–brain barrier. The same way it takes longer for morphine to enter the brain tissue due to this lipid-favouring barrier, it takes longer for morphine to exit the tissue as well.[3] Additionally, how strongly the morphine binds to specific receptors may contribute to its long-acting effects.

Although the dampening of the perception of pain is one of the main effects of morphine on the central nervous system, it goes beyond this as well.

Morphine takes further effect in an area of the brainstem called the mid-brain, where it activates inhibitory pathways that send a signal to a part of the spinal cord instructing it to dampen the activity of pain-transmitting neurons there. The binding of morphine to opioid receptors within the spinal cord also effectively prevents the pain signals from being sent to the brain.

However, it is not only the central nervous system being affected. Morphine also affects the peripheral nervous system, the system of nerves branching out from the spinal cord and brain to the rest of the body, which is responsible for relaying information such as pain signals back to the brain.

In the peripheral nervous system, morphine affects nociceptive neurons (specialized sensory neurons found in areas such as the skin), by binding to their opioid receptors just like they do in the brain, thereby inhibiting neuron activity and not allowing them to communicate their pain sensation to the spinal cord or brain. So, in addition to muting the perception of pain in the brain, morphine additionally is capable of stopping signals of pain from being communicated close to the source of pain itself.

Minutes go by, and you find yourself in an almost dreamlike state. As the feeling of calmness continues to set in, you notice your breathing beginning to slow.

'In…. Out…. . In…… Out………… In……….. . Out……………..In…………………Out…'

Your heartbeat and blood pressure also take a dip, and you start to feel sleepy. You are filled with a sensation of warmth and happiness. The anxiety that so recently gnawed at your brain is now a distant recollection.

When bound to opioid receptors in the brain, morphine suppresses the substance noradrenaline, a neurotransmitter and hormone affecting blood pressure regulation, alertness, wakefulness, stress response, mood and pain perception.[4] This suppression of noradrenaline lowers heart and breathing rate, blood

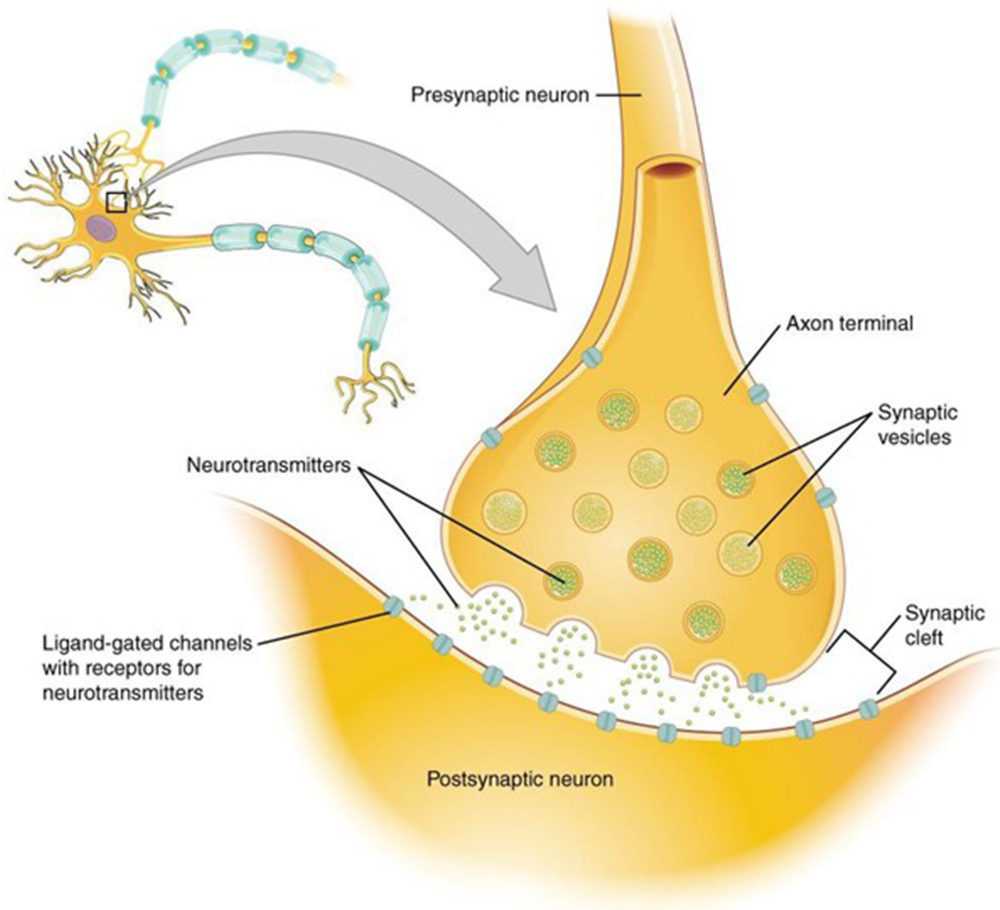

Figure 2. Chemical synapse: anatomy and physiology, https://openstax.org/books/anatomy-and-physiology/pages/preface. Website: https://commons.wikimedia.org/wiki/File:1225_Chemical_Synapse.jpg

pressure and wakefulness in individuals under the effect of the drug.

It is crucial to note there are many concerns to be had when taking morphine and other opioids. Frequent usage of consistently higher doses will cause the body to become increasingly tolerant to it, requiring greater doses to feel the same effects. The brain would respond to constant opioid use by increasing the amount of noradrenaline receptors in the body, thereby increasing sensitivity to even small amounts of noradrenaline. When this occurs, the individual at hand would begin to feel devastating symptoms of withdrawal when not using the opioid, such as fever, stomach aches and vomiting. Not only would it become extremely hard to quit, but, when one tried, it would require months of time, sufficient funds for rehabilitation, financial stability and resources that many people don't have. The path to addiction is far too easy for a drug so common and powerful. For even the strongest, most disciplined people, being warned is not necessarily enough to stop them from accidentally following a path that is dangerous and inhumanely difficult to escape.

But in this moment, all you feel is a potent mix of exhilaration and relaxation, and for the next 4–6 hours, this feeling is all yours. The absence of pain and the overwhelming presence of bliss make everything else a mere afterthought. ■

You can view all the winners from 2022 *and* 2023 *on our website.*

The Science Communication Prize will be back in summer 2024! Stay updated through our website and social media.

References

1. Morphine Addiction: Treatment, Signs & SymptomsDelamere Health. Available from: https://delamere.com/addiction-treatment/morphine-addiction [Accessed August 22, 2023].
2. Chahl LA. Opioids - mechanisms of action. Aust. Prescr. 1996;19:63–5.

3. Taylor DR. The Pharmacology of Fentanyl and Its Impact on the Management of PainMedscape Education. Available from: https://www.medscape.org/viewarticle/518441 [Accessed August 22, 2023].

4. Dellwo, A. What Does Norepinephrine Do in the Body? verywell health. Available from: https://www.verywellhealth.com/norepinephrine-what-does-or-doesnt-it-do-for-you-3967568# [Accessed August 22, 2023].

Author information

My dream is to study biochemistry in university and beyond because I think investigating the science behind complex processes of life, both around and within us, is an incredible lens to perceive the world through. Participating in this competition was a great opportunity for me to learn about what good science communication is, as well as how to apply the scientific concepts I know in a way that makes the knowledge interactive and accessible for everyone. Overall, I'm very grateful for this experience as it has deepened my understanding of how biochemical processes are responsible for the way we perceive life.

