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Parasitic mastermind: Exploring the science of Plaga Araña

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Abstract
In the computer game called Resident Evil 4 (2023), there are a plethora of enemies who have been infected by a fictional parasite called las Plagas. The game features a wide range of different types of Plaga parasites, with a notable example being Plaga Araña. This paper explores this particular parasite's biology and how it is able to control its host. Comparisons will be made to real-world parasites to examine any similarities and differences.

Keywords: *Computer game; Biology; Parasite; Neuromuscular Junction; Plaga Araña; Resident Evil 4*

Introduction
In the game Resident Evil 4 (2023), the enemies have been infected with a parasite called las Plagas [1]. Throughout the game you encounter different types of Plaga parasite, with the most notable being a certain type called Plaga Araña. This particular parasite is notable as instead of infecting and subsequently controlling the individual from within, this parasite can attach itself to someone's back and, utilising tendrils it produces, control them in the same vein as a puppeteer using a puppet (Figure 1). Additionally, they can survive outside of a host unlike the other Plaga parasites [1]. This paper attempts to analyse how this parasite does this and compares it to real-world parasites to see if there are similarities.

Figure 1 – A screenshot taken from the Resident Evil 4 (023) model viewer of Plaga Araña attached to the back of an enemy (Ganado) [1].

Real-word parasites
When looking at real-world examples of parasites, we can compare Plaga Araña to a parasite called *leucochloridium*. *Leucochloridium* is a small flatworm that typically infects land-based snails. If a snail ingests the parasite, it grows, producing structures called broodsacs, which eventually occupy the snails' eyestalks [2]. The parasite can also manipulate the snail's behaviour to make the snail more conspicuous to birds. It can also make the snail even more obvious by pulsating the broodsacs with bright colours, which furthermore makes it easier to spot [2]. Like *Leucochloridium*, Plaga Araña can alter the host's behaviour, but instead of making it more conspicuous to predators to reproduce, it makes the host more aggressive, which can be used to defend against a threat.

Later in this paper, the idea that Plaga Araña may influence the host's behaviour and emotions through the utilisation of hormones is explored. An example of a parasite that utilises hormones is *Toxoplasma gondii.* Studies on this parasite have demonstrated that there is an association between an infection with *Toxoplasma gondii* (toxoplasmosis) and an increase in testosterone levels in humans and some animals [3]. The change in testosterone levels may be linked to an increase in sexual activity of infected individuals, which would lead to an increase in sexual transmission of the parasite. Plaga Araña may adopt a similar mechanism in terms of altering the levels of hormones like testosterone but with the goal of

making the host more aggressive rather than more sexually active with the goal of propagation.

Nervous system

When the Plaga Araña parasite attaches itself to someone's back, it produces tendril-like structures that connect to various parts of the body, but in particular the arms and the head. This is particularly important as it suggests that it is interfacing with the nervous system in some way to make the host's body move. In order to do this, it is likely that it interacts with the brain, more specifically the motor cortex, as this is in charge of sending signals to the muscles via the spinal cord. The motor cortex sends electrical signals to the muscles, or to be more precise, the neuromuscular junction (Figure 2), which causes the release of a neurotransmitter called acetylcholine (ACh) [4]. Acetylcholine then binds to receptors on the synaptic cleft, which generates an action potential. This causes the diffusion of sodium ions into the muscle fibre membrane, causing depolarisation which generates an action potential. This depolarisation releases calcium ions, which produce attractive forces between actin and myosin filaments, which leads to the contraction of the muscles [4]. It's possible that the parasite may also interfere with this process by releasing the relevant ions to cause the desired muscle movement.

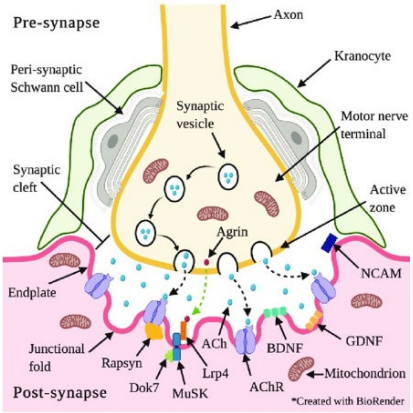

Figure 2 – An image displaying labels and information about the neuromuscular junction and the processes that occur [5].

Cognitive influence

In addition to interacting with the motor cortex, the parasite most likely also interacts with the amygdala and the prefrontal cortex. This is because in-game, when someone is being controlled by Plaga Araña, they are faster and more aggressive. The amygdala generates an aggression response when a possible threat is identified [6]. It is likely the parasite has twisted this perspective to make the person identify the player character as a threat in order to protect the parasite itself. The prefrontal cortex is associated with the control of impulses and is heavily linked to the amygdala, so it is likely that the parasite reduces the activity of this area of the brain so that the amygdala's response isn't inhibited.

Hormone control

Another way in which the parasite may control the aggression of its host is through the use of hormones. The major hormone associated with aggression is testosterone. Testosterone causes increased aggression by binding to androgen receptors in parts of the brain, usually the amygdala, and affects the production of neurotransmitters associated with aggression [7]. This is usually achieved by the conversion of testosterone to oestradiol by the enzyme aromatase. The parasite may also inhibit certain hormones that have an opposite effect to testosterone by releasing antagonistic molecules. Antagonistic molecules usually bind to complementary receptors, which prevent other molecules from binding and prevent the initiation of a reaction. Cortisol is a hormone that interacts with testosterone, which reduces its effectiveness to the point where high levels of cortisol suppress the production of testosterone [8]. Plaga Araña may also release antagonists for dopamine and serotonin, as low levels of these hormones are associated with an increase in aggressive behaviour.

Conclusion

To summarise, the examination of Plaga Araña has revealed many unique insights into how it may go about controlling a person. It shares similarities to that of real-world parasites in terms of its behaviour-altering capabilities and the possible control of the host's hormone levels. These ideas were explored by looking at the ways in which it could affect the brain and nervous system in order to produce a desired response as well as hormone control to induce certain behaviours and inhibit unwanted ones. One thing worth mentioning is that in the game, Plaga Araña only controls people who are already infected with a Plaga parasite, so more research may be needed to determine if it can only control priorly infected individuals. Also, some of the ideas relating to Plaga Araña are theoretical, as there is little to no in-game evidence to suggest that the parasites release hormones into the body, for instance.

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