The Heart Has a Mind of Its Own (*Literally*)

By Ameera Khan

"The brain thinks, but the heart knows"- Joe Dispenza

Have you ever wondered how the heart continues to beat, even when the brain goes quiet? Or why it races when you're anxious? We feel heartbreak in our chest, butterflies before a big moment, and warmth when experiencing love. It's as if the heart somehow *knows* what's happening–sometimes even before our brain finally catches up!

The heart is more than just a hardworking muscle that pumps blood throughout your body. Exciting research shows that the heart actually has its own complex nervous system—a "little brain" —that controls heart function and possibly the way we feel and process our emotions.[1] This nervous system, in scientific terms, is known as the intrinsic cardiac nervous system (IcNS). The IcNS is made up of about 40,000 neurons (also called sensory neurites) embedded in the heart's tissues. These neurons can learn, feel, sense, and remember, and are supported by many other types of cells (i.e. glial cells) that regulate how often the heart beats, responds to stress, and interacts with the brain.[1,3]

Think of the IcNS as a manager of a big company, while the brain is the CEO back at headquarters. The heart's nervous system handles *local* tasks and operations, without needing constant direction from headquarters (the brain). Biologically, this means that the heart can sense, adapt, and regulate itself, even without direct instructions from the brain.

But we all know, no good manager works alone! To keep things running smoothly, the IcNS still stays in communication with a key branch of the body's nervous system known as the autonomic nervous system (ANS). The ANS is responsible for involuntary actions that we don't need to consciously think about such as breathing, digestion, and more excitingly, our heart beating!

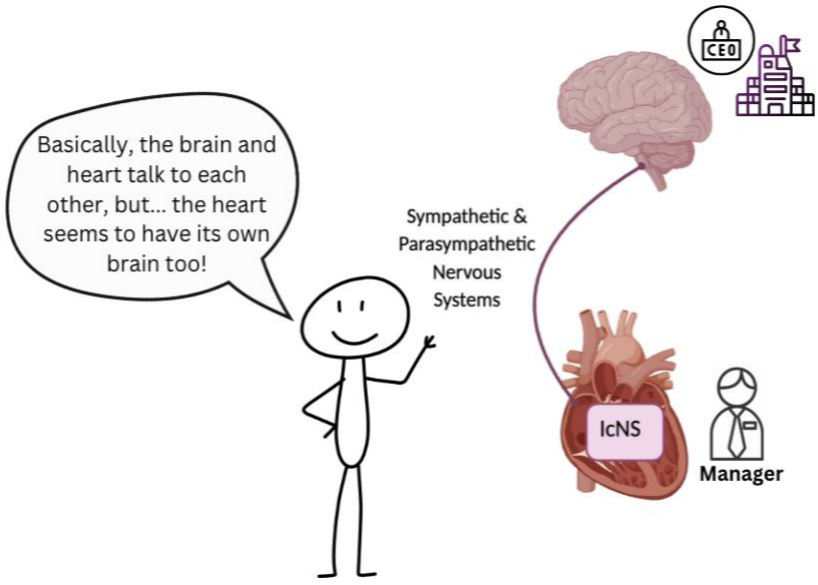

Figure 1. How the Heart Communicates with the Brain

The ANS has two major divisions: the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS).[2,4] Think of the SNS as our "fight or flight" response, kicking in under stress or excitement to speed up heart rate and prepare us for upcoming action.[2] On the other hand, the PNS slows and calms things down, allowing the heart to recover and relax.[2] Putting everything together, we know that while the brain *does* influence heart function, the heart itself is also able to work independently with its own "brain", the IcNS (*Figure 1*).

Aside from regulating its own rhythm, blood flow, and other activities, the heart can also impact cognitive (mind) functions, including decision-making, mood regulation, and emotional processing. In fact, the heart actually sends more signals to the brain than the brain does to the heart.[1] For example, studies suggest that the heart helps shape how we experience pain by sending signals to the brain areas involved in emotion and perception.[1] Even more interesting research shows that the heart can release oxytocin, a molecule sometimes referred to as the "love" hormone due to its important role stimulating feelings of warmth, trust, and social bonding.[1,2] The brain may be the CEO, but the heart is clearly more than just mid-level management!

Today, scientists can take ordinary human blood or skin cells and add specific molecules to convert them into what are known as human induced pluripotent stem cells (hiPSCs). These remarkable cells are capable of becoming almost any cell type in the body, including our favorite—the neurons found in the heart's nervous system! By turning hiPSCs into cardiac neurons, researchers can study the heart's "little brain" in a dish, without needing a living human heart.

Why does that even matter? Well, imagine you or a loved one has a cardiovascular condition like heart failure or an arrythmia (irregular heartbeat). Scientists can use hiPSCs to better understand and potentially treat these conditions. Specifically, they can study how these cardiac neurons develop, communicate with other heart cells, and influence heart rhythm.

Some scientists are even going a step further! They've developed tiny, lab-grown 3D models called sympathetic neuron-innervated cardiac assembloids which combine heart muscle cells and neurons made from stem cells (*Figure 2*).[5] These mini "heart-brain systems" can beat on their own and respond to signals, just like a real heart would when getting messages from the nervous system!

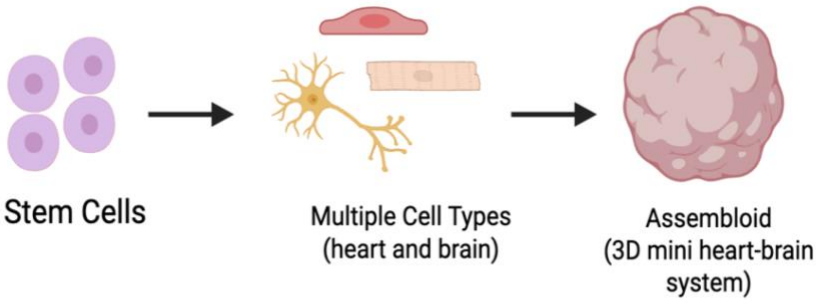

Figure 2. Lab-Grown 'Heart-Brain' Model Using Stem Cells

While these models don't yet include all of the specialized neurons found in the IcNS, they're still an exciting step forward. Just imagine the possibilities—researchers can begin to study how stress signals from the nervous system, and even emotional cues might influence the heart at the molecular and cellular level.[5]

Remember folks: the heart has a mind of its own—and thanks to stem cells, we're finally beginning to understand what it's trying to tell us!

References

1. Alshami, A.M. Pain: Is It All in the Brain or the Heart?. *Curr Pain Headache Rep* **23**, 88 (2019). https://doi.org/10.1007/s11916-019-0827-4

2. Tedoldi, A., Argent, L., & Montgomery, J. M. (2021b). The role of the Tripartite Synapse in the heart: How glial cells may contribute to the physiology and pathophysiology of the intracardiac nervous system. *American Journal of Physiology-Cell Physiology*, *320*(1). https://doi.org/10.1152/ajpcell.00363.2020

3. Tendulkar, M., Tendulkar, R., Dhanda, P. S., Yadav, A., Jain, M., & Kaushik, P. (2024). Clinical potential of sensory neurites in the heart and their role in decision-making. *Frontiers in Neuroscience*, *17*. https://doi.org/10.3389/fnins.2023.1308232

4. Fedele, L., & Brand, T. (2020). The Intrinsic Cardiac Nervous System and Its Role in Cardiac Pacemaking and Conduction. *Journal of Cardiovascular Development and Disease*, *7*(4), 54. https://doi.org/10.3390/jcdd7040054

5. Zeltner, N., Wu, H. F., Saito-Diaz, K., Sun, X., Song, M., Saini, T., Grant, C., James, C., Thomas, K., Abate, Y., Howerth, E., Kner, P., & Xu, B. (2024). A modular platform to generate functional sympathetic neuron-innervated heart assembloids. Research square, rs.3.rs-3894397. https://doi.org/10.21203/rs.3.rs-3894397/v1