



HOW YOUR BRAIN CELLS TALK TO EACH OTHER-WHISPERED SECRETS AND PUBLIC ANNOUNCEMENTS

Mike Ludwig*

Centre for Integrative Physiology, University of Edinburgh, Edinburgh, United Kingdom





NEURON

Cells of your nervous system, called nerve cells or neurons, are specialized to transmit "messages." Imagine that you want to tell your friends something new; you could whisper it into their ears or shout it out loud. This is rather like two forms of communication that occur within your brain. Your brain contains billions of nerve cells, called neurons, which make a very large number of connections with specialized parts of other neurons, called dendrites, to form networks. Neurons have been thought to communicate with each other by passing ("whispering") chemical signals directly through these connections, but now we know that they also can spread messages more widely ("public announcements") by releasing chemical signals from other parts of the neuron, including the dendrites themselves. If we understand how and what neurons communicate with each other, we will have a chance to correct disturbances in communication that may result in altered behaviors and brain disorders.

We know that the human brain is the most complex structure. It has approximately 80 billion nerve cells, called **neurons**. Eighty billion (80,000,000,000)! This is more than 10 times as many neurons as there are

NEUROTRANS-MITTERS

Chemicals used by neurons to talk to each other—we can think of them as "chemical words."

FIGURE 1

A. Some neurons, like this special kind of neuron called a Purkinje cell, look very similar to trees B. C. Neurotransmitters (key) released from the axon terminals only have to cross a very tiny gap (a synapse) **D.** to reach their receptors (lock). However, when they are released from dendrites, their receptors can be far away and need to be reached by diffusion. Purkinje cell image courtesy of Marta Jelitai, Hungary.

people living on Earth. Neurons talk to each other using special chemicals called **neurotransmitters**. Neurotransmitters are like chemical words, sending "messages" from one neuron to another. There are many different sorts of neurotransmitters: some stimulate neurons, making them more active; others inhibit them, making them less active. Neurons control literally everything you do.

THE NEURONS ARE THE BUILDING BLOCKS OF YOUR BRAIN

Neurons come in many forms, shapes and sizes, but it is helpful to think of a neuron like a tree. A neuron has three main parts, the cell body, an axon, and the dendrites (Figure 1). The tree trunk (cell body) stores genetic information (DNA) in a compartment called the nucleus. The cell body also contains the chemical machinery to produce the neurotransmitters that the neuron uses to communicate with each other.

The tree's branches (dendrite, the word déndron comes from the Greek language and actually means "tree") are the parts of a neuron that receive signals. Dendrites were once thought to be like antennae, just receiving signals from other neurons, but, as I explain, they can do more than this.



kids.frontiersin.org

The tree root (axon) is the structure used by a neuron to connect with and talk to another neuron. An axon carries information similar to a cable that carries electricity. When one neuron wants to share a message with another, it sends an electrical impulse, called an action potential, down its axon until it reaches the axon terminal, at the end of the axon. Think of an axon terminal as an airport terminal. An airport terminal is filled with passengers waiting to depart, whereas an axon terminal is filled with neurotransmitters waiting to travel to the next neuron.

WHAT ARE THE DIFFERENCES BETWEEN WIRED AND WIRELESS TRANSMISSION?

When the action potential reaches the axon terminal, some of the neurotransmitters in the terminal are dumped into a tiny gap between the terminal and the dendrite of another neuron. This gap is called a synapse—it is so tiny that it is measured in nanometers or billionths of a meter. The neurotransmitter crosses the synapse and binds to a specialized site, called a receptor, on the other side. Each neurotransmitter binds only to its specific receptor, just as a key fits only in a particular lock. Depending on the neurotransmitter, it either stimulates the other neuron or inhibits, making it either more likely or less likely to fire an action potential of its own. All these happens with very high precision and is repeated again and again. Since the signal is passed at very high speed from one neuron to another (up to 100 m/s or 223 mph; faster than the fastest land mammal, the cheetah, which can accelerate to a speed of 29 m/s or 64 mph), this kind of communication between neurons is sometimes called "wired transmission." The neurotransmitters pass "whispered secrets" directly from one neuron to another; they carry a message that matters only at a particular time and place. One way of thinking about "wired transmission" is to think about a light switch, which switches a particular light bulb on or off.

NEUROPEPTIDES

A special type of neurotransmitter. They influence activities in the brain and body, for example regulating a person's energy level. Some neurotransmitters, especially one kind called **neuropeptides**, are different. Neuropeptides are released from many parts of a neuron, including the dendrites. Rather than being released into the tiny synapse between an axon terminal and another neuron, they are released into the fluid that fills the spaces between neurons, and they diffuse through the brain to reach receptors that are on distant targets. One way of thinking about diffusion is to consider making your way through a forest (Figure 2). To go from one point to another when no trees are around would be very simple and fast. Once you have a lot of trees, going from one point to another would take much longer time, because you must go around the trees. So this sort of signaling is much slower than signaling at synapses, but eventually the neuropeptides will reach most parts of the brain. However, only brain areas that have the right receptors can respond to the neuropeptides. So release of neuropeptides by dendrites, like Wi-Fi, is a wireless signal—these messages are "public announcements"

FIGURE 2

Neuropeptides (key) are released into the space between neurons (trees) and diffuse through the brain to reach receptors (locks) that can be on distant targets. Consider diffusion like making your way through a forest. The time it takes to reach your lock (receptor) depends on how many trees (other neurons or cells) you have to go around.

HYPOTHALAMUS

The hypothalamus is a brain region that regulates functions like thirst, appetite, and sleep.

PITUITARY GLAND

The pituitary gland is located in a small, bony cavity at the base of the brain. It is connected to the hypothalamus. It secretes hormones regulating many different bodily activities.



that are not sent from one cell to another, but from one group of neurons to another group of neurons [1].

OXYTOCIN AND VASOPRESSIN CAN AFFECT BEHAVIOR BY "WIRELESS" SIGNALING

Let me use another example. The neuropeptides, oxytocin and vasopressin, are made by large neurons in the **hypothalamus**, a part of the brain that is important in regulating many physiological processes of the body. These large neurons have one axon that goes all the way to a specialized gland, the **pituitary gland**, which is attached to the bottom of the brain. From there, the neuropeptides are released from the axon terminals directly into the blood. Oxytocin travels through the body and has a role in childbirth and breastfeeding. Vasopressin affects blood pressure and regulates the body's water balance through the kidneys. But both neuropeptides are also released into the brain, where they control several sorts of behavior. For example, oxytocin helps a mother to bond with her child, and vasopressin affects memory and aggression. However, the brain areas that control these behaviors are sometimes far from the cells that make the neuropeptides. Some of these areas have the right receptors but no axons and terminals nearby, so that "wired" signaling by oxytocin and vasopressin cannot occur.

The oxytocin and vasopressin released from the axon terminals into the blood cannot re-enter the brain because of a strange structure called the blood-brain barrier. Think about it, when you get sick, you do not want bacteria or viruses to invade your brain! The blood-brain barrier is a layer of cells keeping the brain safe from pathogens, toxins, and other molecules circulating in the blood. It prevents invaders from entering the brain.

However, oxytocin and vasopressin are also released from the dendrites of the neurons, directly into the brain. Scientists have discovered that the release of neuropeptides from dendrites (into the brain) and from axons terminals (into the blood) can happen independently. Release of vasopressin and oxytocin from the axon terminals is controlled by action potentials, similar to the neurotransmitter release triggered in all other neurons. However, some chemical signals in the brain can stimulate neuropeptide release from the dendrites *without* triggering action potentials. Producing release in these different ways allows neuropeptide effects in the body and the brain to be regulated separately. For example, as well as having effects on the body, such as childbirth and breastfeeding, oxytocin also stimulates the mother's childcare and bonding—actions of the brain. This makes sure that the newborn receives all that is urgently needed: food and love (Figure 3) [2].

HORMONES

Hormones are special chemicals that the body makes to help it do certain things like growing up and going through puberty, which is when you begin developing into an adult. During this time, your body is loaded with hormones that tell it that it is time to start changing.

FIGURE 3

Oxytocin is released into the blood from axons in the pituitary gland (blue arrow) and into the brain (white arrows) from the dendrites of neurons in the hypothalamus (red area). Oxytocin acts both in the body and in the brain to make sure the child gets food (oxytocin's action on the body) and love (oxytocin's action on the brain).

ARE NEUROPEPTIDES SIMILAR TO HORMONES?

Release of neuropeptides by the dendrites of neurons is very similar to the release of **hormones** elsewhere in your body. Hormones are the chemical messengers released by glands and transported by the blood to distant target cells. So, hormones can stimulate cells that are located far away from the glands where they are produced. There are many different



kids.frontiersin.org

hormones, and they have lots of different functions in the body. For example, prolactin, another hormone released from the pituitary gland, travels to a mother's breast where it stimulates the production of milk for breastfeeding. This process of "wireless signaling" by hormones is like the signaling by neuropeptides within the brain—so neuropeptides could be called "brain hormones."

WHY IS IT IMPORTANT TO UNDERSTAND NEUROTRANSMITTER SIGNALING?

Some of the behavior disorders hardest to treat, for which new therapies are urgently needed, affect behaviors in which vasopressin and oxytocin are involved [3]. As mentioned above, oxytocin is involved in childbirth, breastfeeding, and the mother's behavior toward childcare. But oxytocin is also important for the child to develop and maintain complex interactions with others. Some children with **autism** often have difficulties in understanding and responding to those interactions, and scientists are trying oxytocin as a potential treatment (if you want to learn more about this, read the article written by Daniel Quintana and Gail Alvares in the Frontiers for Young Minds online library) [4].

Other examples include disorders associated with stress and anxiety, disorders of eating, disorders of substance misuse (including alcohol misuse), and disorders of sexual behavior. These are major health problems with a considerable impact on humans. By better understanding how brain cells and neuropeptides interact, we may find ways to control some of these disorders and improve the quality of our lives.

ACKNOWLEDGMENTS

I would like to thank my friends and colleagues at work who commented on the manuscript, especially my friends David and Gareth who made sure that I used the right words understandable for kids. I would also like to thank Márta for the Purkinje cell image.

REFERENCES

- Ludwig, M., and Stern, J. E. 2015. Multiple signalling modalities mediated by dendritic exocytosis of oxytocin and vasopressin. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 370(1672):20140182. doi:10.1098/rstb.2014.0182
- 2. Ludwig, M., and Leng, G. 2006. Dendritic peptide release and peptide-dependent behaviours. *Nat. Rev. Neurosci.* 7:126–36. doi:10.1038/nrn1845

AUTISM

Many kids who have autism have trouble understanding what other people are thinking and how they are feeling. They might act in a way that seems unusual, and it can be hard to understand why they are acting that way.

- Neumann, I. D., and Landgraf, R. 2012. Balance of brain oxytocin and vasopressin: implications for anxiety, depression, and social behaviors. *Trends. Neurosci.* 35:649–59. doi:10.1016/j.tins.2012.08.004
- Quintana, D. S., and Alvares, G. A. 2016. Oxytocin: how does the neuropeptide change our social behaviours? *Front. Young Minds* 4:7. doi:10.3389/ frym.2016.00007

SUBMITTED: 19 January 2017; ACCEPTED: 11 July 2017; PUBLISHED ONLINE: 26 July 2017.

EDITED BY: Lesley K Fellows, McGill University, Canada

CITATION: Ludwig M (2017) How Your Brain Cells Talk to Each Other—Whispered Secrets and Public Announcements. Front. Young Minds 5:39. doi:10.3389/frym.2017.00039

CONFLICT OF INTEREST STATEMENT: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

COPYRIGHT © 2017 Ludwig. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) or licensor are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

REVIEWED BY



SARIT, 14 YEARS OLD

Hello! My name is Sarit and I am a 14 years old girl from Canada. Some of my hobbies include playing the cello, reading innumerable books, and writing. During the winter, I love to go snowboarding with my family and friends. I enjoy learning new things, especially when they are related to Math or Science, my favorite subjects at school.

AUTHOR



MIKE LUDWIG

I was born and educated in Germany. Now I am professor at the University of Edinburgh in Scotland, UK, leading a research group that researches the fundamental mechanisms of neuropeptide release and its actions on neuronal networks and behaviors. In addition to research, I like to play with my dog (I used to have a sled dog team of six huskies) or travel to go on photo safaris. *mike.ludwig@ed.ac.uk