The Body's Alphabet

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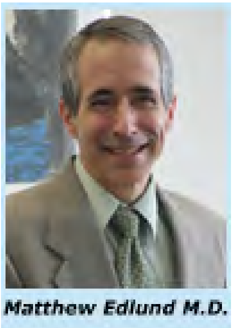
It's hard to conceptualize how the body's giant information network connects and communicates. Yet we can begin to understand by watching how neurotransmitters, information molecules prominent in the nervous system, create completely different meanings depending of where they are found.

There are hundreds of neurotransmitters. Some, like serotonin, have reached public fame through pharmaceutical advertising.

Nerve cells create information through a simple act - firing or not firing. Every time they fire, they pop out at least two different kinds of neurotransmitters – fast and slow. Fast neurotransmitters, like glutamate, generally operate quickly, with effects lasting milliseconds. Others, like serotonin and epinephrine, move throughout the central nervous system, engaging large cell networks. Their actions may last from tenths of seconds to minutes.



Other communication molecules, like coricosteroids or growth hormone, often produce effects lasting minutes to days, acting throughout many parts of the body. Looking only at the dimension of time, researchers see at least four temporal levels of neurotransmitters, with effects varying from thousandths of seconds to days.

Serotonin is an important neurotransmitters with critical functions in keeping the brain awake and alert. Drugs like SSRIs, including prozac and zoloft, prevent reuptake of serotonin, leaving it to act a bit longer at the nerve cell's business end, the synapse. Many a depressed person now will come into a doctor's office and say "I want to increase my serotonin levels."

I ask them where they think most of the body's serotonin is. "The brain?"

No, it's the gut. More than ninety percent of body serotonin is found in the gut. Is the gut then the site where antidepressants work?

Drug company advertising has not mentioned that increased serotonin activity is what drives the hallucinations of LSD and the weird "love of humanity" sensations people experience when taking the drug Ecstasy. They don't advertise that excessive serotinergic action can produce the serotinergic syndrome, leading to nausea, palpitations, hypertension, fever, sometimes death.

That's because serotonin's effects in the brain are just one bit of its overall story. Serotonin works through attaching to serotonin receptors. In the brain, if enough serotonin attaches in a space of time to enough receptors, the nerve cell will fire. However, as of this writing there are at least seven different **families** of serotonin receptors. They produce different results in different parts of the body.

There are also dozens of different serotonin receptor subtypes. Many of the most successful anti-nausea medications block serotonin receptor type 3 receptors present in the gut.

These many different receptors help explain why epinephrine in the brain often produces the opposite effect on blood pressure than epinephrine outside the brain. It's why cholecystokinin, the "hormone" that pushes the gut to secrete enzymes to break down fat and protein, also modulates opiate addiction, and why histamine keeps the brain awake but also pushes out acid in the stomach.

The molecule may be the same. The effects are not.

It's almost as if every organ was a different country with a different language. The alphabet of neurotransmitters has different meanings in each.

Yet the truth is both more interesting and more complicated. There are far more information molecules in the body than neurotransmitters. In fact, there are thousands. There are the famous ones, like the hormones cortisol and thyroid, but there are others rarely considered information carriers, like ATP, the central molecule in cellular energy processes. Because these molecules often have different effects in different end organs, they can be thought of as letters in the alphabet of not one but many languages.

English has 26 letters. Yet the body has thousands of different "letters" that can be used, as an A or C is used in German, French, Romansh, or Italian, to create wholly different words, paragraphs, and books.

Evolution is slow but its results can be smart. Molecules are used then reused and rebuilt, over and over and over. These molecules often perform many, very different information roles. Cholecystokinin can make your gall bladder contract **and** change your response to morphine. Serotonin can make your duodenum move, provoke hallucinations, or increase your impulsive desire to eat ice cream for dinner.

Systems biology is beginning to make sense of all these different languages. Much as a nerve cell works by firing or not firing, computer code ultimately depends on a series of zeros and ones. The same machines that convert the ideas you are reading in this newspaper are being pressed to understand the thousands of different letters of the body's alphabet and its many languages. Fortunately for us, those many "languages" talk to each other all the time.

We are the network of those near infinite small events. Even little snatches of knowledge, imperfectly understood, like the interconnected actions of food, activity, and rest, can make our most basic human actions more effective, enjoyable, and useful.

Getting to read those languages should be a lot of fun.

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