CELLULAR NEUROTRANSMITTER/HORMONE COMMUNICATIONS IN THE FLUID ENVIRONMENT OF THE BODY†

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Of central importance to Emanual Swedenborg's philosophy of the Animal Economy and the communication between the soul and the body are two primary concepts. One concept is that the body is given its shape by a vast and interconnected series of fibers. The second is that within this fibrous matrix there flows a series of fluids. In the *Economy of the Animal Kingdom* he states:

> We may thus understand the course of the circulation of the animal spirits; namely, that it is from the cortex into the universal fibers, from the fibers into the blood, from the blood into the brain, and so back to the cortex.
>
> I do not think there is any more excellent or noble science in the universal animal kingdom than the science of the circulation of the spirituous fluid. For this fluid glances through every point, and continues, irrigates, nourishes, renovates, forms, actuates, and vivifies everything whatever in its limited universe. (EAK, n. 168)

In the following, I will be presenting a general overview of communications within the body and the central role played by fluids as Swedenborg describes it. I will attempt to relate his ideas to modern concepts and discoveries.

Cells and fluids

To discuss fluids and communications we should first review the communicators, namely the cells that make up the body and the fluid

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world in which they live. The cell is a tiny living entity composed essentially of a highly complex fluid enclosed by a highly complex membrane. Every cell (except the red blood cell) contains a nucleus. The nucleus is also a special fluid enclosed by a membrane (Greep and Weiss 1973). Inside the nucleus are, among other things, the chromosomes. The enveloping membrane of the cell, its outer skin, is extremely complex, containing a large number of specialized molecules in a highly ordered configuration. A great deal of research is now being done to try to understand how the cell forms and maintains this complex surface (Daniels et al. 1990, 99-108; Sabatini, Louvard and Adesnik 1991, 575-579). For as small an area as it is, there exists a tremendous heterogeneity and complexity over this surface. Many articles are now appearing that suggest that a helical fibrous matrix within the cell is responsible for this organization. This is the more interesting for its contrast to the current theory on the cellular membrane, that it is essentially a fluid made up of lipids in which the various known protein structures float freely around. In discussing communications we will need to refer to certain specializations of the surface, one for acting on, and the other for sensing the aqueous environment that surrounds it. These, it will be seen, may be analogous to Swedenborg's internal sensories and motories. But these specializations are only two of many that each cell in the body creates. It is important to note here that the cell is in control of, and is responsible for, creating and maintaining the structure of this all important outermost membrane.

The body is an organization of trillions of cells. These cells group together into organs such as the liver or the skin, and the cells that make up each organ resemble, in a functional sense, the organ as a whole. Each cell can be thought of as a microcosm with the organ as a relative macrocosm (EAK, vol. II, n. 106). For the most part the cells are not physically bound directly to each other although this is the case in many circumstances. They remain in there proper places in the body by using special adhesion molecules on the surfaces to associate with the universal fibrous matrix or basement membrane.

Between the cells there constantly flows a fluid called the interstitial fluid. Each cell is close to a blood capillary with its ever flowing supply of oxygen and nutrients. Lymph vessels also pass nearby. The cells act within this fluid environment from a type of freedom in which they sense the needs of the community and respond in ways that are natural for them. Cells are capable of making some decisions on their own and are being viewed by modern science less and less as passive parts of a vast chemical circuit and more and more as active members of an intellegent organization.

The fluids that are washing through this cellular community have a particular order described by Swedenborg. The following discussion will refer to the three primary fluids in the body that are contained by vessels (i.e. blood, lymph and the ependymal layer enclosing the cerebro-spinal fluid). In another quote from the very beginning of volume I of the *Economy of the Animal Kingdom*, Swedenborg writes:

> This subject [of the flow of fluids; see also n. 38], however, which is of the utmost importance and deserves a voluminous explanation, ought not to be lightly dispatched; but as we cannot here enter more at large into its consideration, the reader must be content for the present simply to keep in mind the leading points I have just enumerated… (EAK, n. 39)

The points referred to above are: 1) that a special spirituous fluid is created in the brain by the cortical glands. 2) This fluid is added to the fluid that is within the ventricles of the brain. The fluid in the ventricles is a purer serum drawn by the brain from the red blood. 3) After mixing with the spiritous fluid, this fluid is returned to the blood by two means, via the subarachnoid space in the membranes surrounding the brain, and by flowing down through the nerves, into the body and thus back into the red blood. Thus, "the (cerebro-spinal fluid) joins the (lymph) to produce the blood"(Rosen and Chaudhuri 1983, 28-30; Leeds, Kong, and Wise 1989, 144-146).

The preceding description of the relationship between the three fluids (not including the spirituous fluid) is in substantial agreement with modern concepts (see Editorial Note VII in volume II of *The Brain*). The cerebro-spinal fluid is believed to be produced from two sources. Sources for this fluid are the special organs in the ventricles of the brain called choroid plexuses. The other source is the capillary bed running through the tissue of the brain. In both the capillaries and the choroid plexus there exists a highly selective barrier between the cerebro-spinal fluid and the blood itself. This barrier, called the blood-brain barrier, draws most of what the brain requires from the blood, and is capable of excluding unwanted substances. This selectivity includes such things as maintaining different salt concentrations in the blood and the cerebro-spinal fluid. Swedenborg refers to this in *Economy of the Animal Kingdom*, Volume II n. 118:

> I say that the substance of the cortex attracts the purer essences or animal spirits from the arterial blood of the brain, but not from its concomitant serum, and transmits them into the subtlest passages of the fibers.

The fluids from both of these sources are mixed in the ventricles to form the cerebro-spinal fluid. The major difference between the two sources is that the fluid from the choroid plexus flows directly from the blood stream into the ventricles or mixing chamber, while that from the capillary bed passes first through the substance of the brain itself. Once created, the cerebro-spinal fluid flows from within the ventricles down towards the spinal chord. Just before entering the spinal chord a large amount of the fluid flows out through a foramen (foramina of Magendi) just under the cerebellum and into the sub-arachnoid space surrounding the exterior of the brain. There are other, lesser means of egress for this fluid into the sub-arachnoid space. In the sub-arachnoid space it is re-absorbed into the blood via the arachnoid villa and returns toward the heart. The remainder does two things: part flows down the sub-arachnoid space of the chord and comes back up, and part enters into the nerves and flows out into the body by means of them where it eventually joins the lymph and then flows back to the blood (Leeds, Kong and Wise 1989, 144-146; Martin, John, and Dennis 1988, 1218). This second means of return will not be found in text books of physiology due to the recentness of this discovery.

The lymph arises from fluid leaving the veinous capillary beds throughout the body. This fluid constantly leaves the blood vessels along with various types of cells which are a part of the immune and inflammatory systems. This fluid becomes part of the interstitial fluid that exists between all cells. Fluid also enters the interstitial space as a result of digestion from the stomach, small and large intestines. There are a great many vessels of the lymph system surrounding those organs and they receive from the interstitial fluid the nutrients, fats and the water that are absorbed through the walls of the digestive tract. Further, as mentioned above, the cerebro-spinal fluid flows into the interstitial fluid from the nerves and is then added to the lymph. This fluid collects in the lymph vessels which flow together from all over the body and eventually rejoin the blood stream as it returns to the heart through the thoracic duct.

In addition to the presence and relationship of the fluids it is also important to realize the extent to which this environment or atmosphere is changing. The heart pumps out approximately 1.3 gallons of blood per minute. The brain's entire content of cerebro-spinal fluid is replaced five times per day. Approximately 1.5 quarts of lymph flow into the blood stream each day. Every part of the body is in a state of constant flux with respect to the fluid environment and through all this flux of change the trillions of cells manage to maintain communications.

Communication

The human body is in a state of constant communication which continues uninterrupted until death. Communication occurs in many ways. The movement of a "hair" cell such as in the cochlea of the ear can initiate a signal to the central nervous system. An increase in acidity of the blood can result in a change of activity in some cells such as the respiratory cells in the brain. Some cells are sensitive to being stretched, others to physical touch, and others to changes in pressure. But by far the most prevalent form of communcation within our bodies occurs by the deliberate and controlled release of special substances by one cell (or group of cells) and the intelligent detection of those special substances by other cells (Nicoll, Malenka, and Kaue 1990, 513, 564). In other words, when a cell has something to say, it says it in a language of molecules which it releases into the surrounding fluid environment. The release is done through special "motories" called presynaptic membranes that are created and maintained in part by an array of helical protein filaments.

When a cell needs to know something, it listens to that same fluid enviroment with specialized sensories that it elaborates on its own surface.

For each molecule in this molecular language there exists a special type of sensory. The cell can build these sensories, which are composed of at least partially helical filaments, on its surface. The fibers of the sensories are believed to actually move as part of the process of "sensing."

To explain a little better how this works we may look at some specific examples of communication. In the first example, we will look at a nerve-cell-to-nerve-cell connection, second a nerve-cell-to-muscle-cell connection and lastly a nerve-cell-to-monocyte connection.

Two nerve cells communicate with each other by means of a structure called a synapse. A synapse is usually referred to as a connection between nerve cells, but it is not a physical connection. The two cells are always separated by a measurable (albeit exceedingly small) space. The space in the area of the synapse is called the synaptic cleft. The "connection" consists of a specialization on the surface (mentioned earlier) of both cells. On the sending cell, the specialization enables the nerve cell to act by releasing exactly measured amounts of a substance called a neurotransmitter which is part of the molecular language also mentioned above. In addition, there are special molecules that are capable of re-capturing the neurotransmitter molecules once they have been released. This contributes to clearing the neurotransmitters out of the environment of the synaptic cleft after their job is done. The flow of fluid over and between the cells also accomplishes this. The other cell, the receiving cell, creates what I earlier referred to as a sensory. This is a group of molecules called receptors which are associated together and which are capable of binding or latching on to the neurotransmitters. Whenever the receptors bind a transmitter molecule, they signal the cell that they have recieved a transmitter by altering their shape and thus affecting the state of the cell. The cell makes a decision as to what action to take based on a number of factors most of which remain unknown but are believed to include which receptors are affected and the overall number of affected receptors. If it decides to act, it will then generate a signal to the other cells that it is responsible for signaling to. Any one nerve cell may have thousands or even hundreds of thousands of these sensories on their surface.

In the case of a nerve cell that is associated with a muscle, the nerve cell does not attach to the muscle. It draws very close to the muscle and forms a specialization on its surface, again for the purpose of releasing carefully measured amounts of the transmitter molecules into the immediate vicinity of the muscle cell. This specialization of the nerve in conjunction with that of the muscle cell is called a motor end plate. For its part, the muscle cell creates special sensories on its own surface in this same area. These sensories are capable of detecting the presence of the transmitter molecules that are released by the neuron and are free in the fluid of the cleft. This "connection" is called a neuro-muscular junction. Again the two cells are separated by a fluid-filled gap. The two cells are free to modify the fluid atmosphere and to detect atmospheric changes independently of each other. The fluid within the gap is constantly changing. Whenever the nerve cell "fires" or releases its transmitter molecules into the cleft, the sensories on the muscle cell detect this. As a result, if conditions are right, the muscle cell will decide to contract and the muscle as a whole will move. How much the muscle contracts and for how long is dependent on many factors. One such factor appears to be how much of the transmitter molecules are released by the neuron and how long they remain in the cleft.

The last example is a look at the association between a nerve cell in the pituitary gland and a white blood cell that is a part of the body's immune system (Martin, John, and Dennis 1988, 1218). In this case, the nerve cell is called a neurosecretory cell because it releases its special transmitter molecules directly into the blood stream instead of the interstitial fluid between two cells. When this occurs the transmitter molecule is called a hormone and it is carried rapidly throughout the body by the blood. The other cell in this case is termed a monocyte which is one of the many white blood cells associated with the immune response. The monocyte circulates in the blood stream until called upon to fight an infection. As in the other examples, the monocyte has special molecules on its surface called receptors. Unlike the other examples though, the receptors are not collected into one area as a special sensory area but are rather spread out over the entire surface of the cell. But the receptors function in a similar way. When the hormone is released into the blood by the neurosecretory cell, all of the billions of cells in the blood stream at that time experience it. But not all of them are capable of recieving it as intellegent information. The monocytes can recieve this hormone and make sense of it as a result of their receptors. This type of communication takes place constantly and in the presence of a free flowing and rapidly changing fluid atmosphere. The monocyte, when it has detected the presence of the hormone, will release substances that communicate with other white blood cells to coordinate an effective immune response to an injury or infection.

The preceding examples are but a few of the countless numbers of relationships existing between different organs and cells of the body. The things that they have in common are modifications of the fluid atmosphere, and the fact that the communicators are in a state of freedom, or independence from each other. One of the differences that we have seen is which of the fluid atmospheres is used by the cells. In the case of the nerve-cell-to-nerve-cell communication and the nerve-cell-to-muscle-cell, the interstitial fluid was used while with the neurosecretory and monocyte communication the blood was used.

In summary we have seen that the human body is a cellular and highly fluid, dynamic structure. The cells which are communicating with each other exist as essentially independant entities within the fluid atmosphere. The fluid constitutes the body's general atmosphere which is divided up into a series of separate atmospheres, those being a series of three vessels containing fluids: the cerebro-spinal fluid, the lymph and the red blood. Further, the modern view of the circulation of these fluids is in agreement with the system that Swedenborg described over 200 years ago.

We have seen that most communication occurs by means of these atmospheres. Communication therefore depends on the state and quality of the cells and the state and quality of the atmospheres.

Failure in communication

Now it is possible to look at some situations where the communication process fails and what happens as a result. In the *Rational Psychology* Swedenborg refers to states of insanity as follows:

> The various kinds of insanities, which are infinite in number, arise from the states of the sensories being so perverted that they enact no changes save such as are irregular and are inharmonious with the pure intellect… (R. Psych., n. 158)

And in another place:

> Naturally, the animus depends upon its intellectories and the common form of the intellectory; but externally it depends also upon the state of the purer blood or animal spirit. If these become diseased, the mind is wont to be insane, nay to become delirious…
> (R. Psych., n. 427)

These two quotes represent Swedenborg's general idea that diseases result from disturbances of the fibers or of the fluids. The work *Economy of the Animal Kingdom* goes into great detail concerning the numerous diseases of man. We can compare this to an example of a disease of the central nervous system as understood today.

Anxiety is a state of mind experienced by all persons. When experienced in a mild form, anxiety encourages us to fulfill our responsibilities to ourselves and to society for both preservation and promotion (personal communication with Dr. James Pendleton). But sometimes an imbalance can occur within the brain which can take a normal process such as anxiety and distort it into a detrimental or even devastating problem.

Although the ultimate cause of anxiety is not known, much is known concerning the neurochemical processes that contribute to it. It has been found that the oral administration of the drug benzodiazepine (personal communication with Dr. James Pendleton) in various forms reduces levels of anxiety in patients with whom anxiety has reached pathological proportions. Further, important aspects of the molecular actions of the benzodiazepine drug have been discovered. The process in question can be summarized as follows, namely: 1) There are nerve cells in a nucleus of the brain called the Locus Ceruleus whose signal transmissions are associated with states of anxiety. 2) It has been found that if these cells do not stop signaling after an appropriate time, the state of anxiety does not subside but instead continues and can even increase. The mechanism that normally causes them to stop signaling is based on "recurrent axon collaterals," that is, axons which put out a branch which circles back to the parent nerve cell and signals that cell to stop. 3) The feedback axon collaterals have failed to inhibit the parent neurons and so the nerve cells continue to signal inappropriately (see above quotation from *Rational Psychology,* n.

158). The neurotransmitter used by these neurons is called Gamma Aminobutyric Acid. The failure of these neurons to stop signaling may be the result of insufficient GABA being released from the pre-synaptic membrane or an alteration in the receptor (sensory) functioning. It turns out that the GABA receptor also recognizes the benzodiazepine drug and binds it. When benzodiazepine is bound to the receptor, it greatly increases the signaling power of the GABA neurotransmitter. This increase can act to offset the reduced effect of GABA and restore normal functioning to the system. Thus a modification of the fluid environment resulted in a cell not sensing proper signals and so acting in an inappropriate manner.

A similar process occurs in certain types of depression. In these cases, the fluid atmosphere is lacking in serotonin which is another neurotransmitter. When cells are expecting to receive serotonin with their receptors and fail to do so, they refrain from signaling the other cells that they are otherwise supposed to communicate with. It has been found that the lack of neurotransmiter is not the result of signaling neurons releasing the molecules but rather that an enzyme called monoamine oxidase is destroying them before they can be sensed by the receiving neurons. Thus again, there is an improper modification of the fluids which results in a failure. The treatment for this to date has been to add a chemical to the fluid that stops the monoamine oxidase enzyme from functioning. This allows the serotonin to diffuse out into the environment and consequently be sensed by the proper receiving nerve cells. Of course, the normal action of the monoamine oxidase is to clear the fluid of the serotonin molecules after they have done their work. With the addition of the monoamine oxidase inhibitor, this function is no longer being performed, which creates certain consequences which are called side effects. But these side effects are accepted as less of a problem than the depression itself.

Conclusions

1) That Swedenborg's vision of the physiology of the human is, in very many respects, close to that which is accepted today. Swedenborg was able to follow the thread of truth through the maze of ideas in his time and assemble many which have withstood the test of time. 2) That the body is created out of so many centers, these centers being the least effigies of the

larger organs. Also that these centers are separate, independent and yet in such perfect communication that they act as one. 3)That these centers are inmost or least sensories and motories which are dependent upon their fluid environment. Swedenborg stressed the concept that there exists an extra-vascular flow of fluids which has since been borne out, including the concept that the cerebro-spinal fluid returns to the blood via the nerves and lymphatics. Finally, 4) that this all-important fluid environment occurs in a series of fluids and that it is upon these fluids that communication depends and is, therefore, the ultimate means of uniting the many individual centers into the whole. ☐

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