New Theory, Compliance Is Key To SM & Alzheimer's

The journal Medial Hypotheses, as the name implies, is a place for doctors, scientists, and researchers to publish interesting ideas they may have that are not yet provable with experimental evidence. The articles are very theoretical and can be difficult to follow for lay people, but sometimes they are worth the extra effort.

In the June, 2004 issue of the journal, Dr. Grant Bateman, of the Department of Medical Imaging at the University of Newcastle, Australia, published his hypothesis on how compliance and impedance are critical not only in how syrinxes form in the spinal cord, but in the development of Alzheimer's disease as well.

What are compliance and impedance you ask? Good questions, and to understand Bateman's theory, we first need to understand some fluid dynamics concepts and how they apply to systems we are more familiar with: the brain, spinal cord, and the flow of cerebrospinal fluid (CSF).

Fluid dynamics, the study of how fluids behave under different conditions, describes how a fluid - such as water or CSF - flows in two distinct ways (see Figure 1). First is non-pulsatile, or steady-state, flow. As the name implies, steady-state flow refers to the situation when a fluid is flowing at a constant, steady rate, much like the water that flows through a garden hose once the hose been filled with water. There is a constant, steady stream of water which comes out of the nozzle.

The second component, pulsatile flow, refers to a flow which is not constant, but rather changes over time, or pulses. If you were to pump water from a bucket (or wet basement) through a hose with a hand pump, the water might spurt out of the end of the hose unevenly. This is an example of pulsatile flow.

Turning back to the steady flow of water through the garden hose in the first example, we all know that if you pinch the hose at some point, you restrict the flow of the water. In fluid dynamics, by pinching the hose, you are creating resistance to the flow. In the case of a steady-state flow, resistance is related to the size of the vessel the fluid is flowing through. The smaller the opening, the harder it is for a volume of water to flow through it.

Turning to our second example, the equivalent of resistance for pulsatile flows is called impedance. It turns out that impedance is related to how compliant - or flexible - the vessel is that the fluid is flowing through. Technically speaking, compliance is a measure of how much a container changes in volume in response to a change in pressure. A balloon, which can be expanded simply by blowing air into it, is very compliant because its volume expands in response to the increased pressure of the air inside.

In contrast, a hard, rigid container, which is not compliant, will not expand when air is forced into it. With pulsatile flow, compliance is a measure of how well a vessel can handle the flow peaks, or pulses. A compliant vessel will allow the fluid to flow more freely, even though there are peaks and valley. A less compliant vessel, because it can't expand to account for the pulses, will restrict, or impede this type of flow (see Figure 2).

Why is this detour into fluid dynamics important? Because the brain and spinal cord - the land of Chiari and syringomyelia - are hotbeds of fluid flow, pulsatile fluid flow to be precise. There are three types of fluid to consider in this region. First, the brain and spinal cord are bathed in cerebrospinal fluid which flows in the sub-arachnoid space beneath the dura/arachnoid and above the actual brain and spinal tissue. Second, blood vessels and arteries run through the brain and spinal cord, carrying blood to and from the region. Finally, interstitial fluid - fluid that exists in the spaces between the actual tissue cells - flows, often on the outside of the blood vessels and arteries.

When the heart beats, blood is forced into the brain compartment. Since the skull is fairly rigid, the increased volume of blood forces CSF (and interstitial fluid) out of the skull and into the spinal area. In the second half of the cardiac cycle, the blood flows back out and some CSF goes from the spine to the skull area. A Chiari Malformation physically blocks this and restricts the natural flow of CSF. While many doctors now focus on the flow of CSF across this space as an indicator of the disease, the exact nature of it's relationship to symptoms and the development of a syrinx is not yet understood.

Bateman points out that since the heart is beating like a pump, the flow of these fluids is not steady, but changes over time and is pulsatile in nature. Since the fluid flow is pulsatile, the compliance and impedance of the system become important parameters in understanding the situation. Bateman suggests that in cases where a Chiari malformation is blocking normal CSF flow, the compliance in the spinal area is lowered. This in turn impedes the natural outflow of blood and interstitial fluid from inside the spinal cord tissue into the sub-arachnoid space. Since the interstitial tissue flows in a pulsatile way in response to the heart beating, it requires the tissue (or vessel) around it to have normal compliance. If this compliance is reduced, the fluid can not flow out of the spine and a syrinx begins to form.

Key Points

1. The cardiac cycle drives blood, CSF, and interstitial fluid into and out of the brain and spinal area
2. The outflow of these fluids from the brain to the spinal area is pulsatile
3. Low compliance causes impedance to the pulsatile outflow
4. Paper hypothesizes that a Chiari Malformation creates a pressure difference between the skull and the spine area
5. This affects the blood vessels in the spinal cord itself and prevents interstitial fluid from naturally draining out of the spine
6. This fluid then collects and forms a syrinx
7. Paper also speculates that as people naturally age their brain becomes more rigid and loses compliance; this results in restricting the flow of interstitial brain fluid and the build-up of beta amyloid, causing Alzheimer's
8. If compliance and/or impedance can be correlated with clinical results, it could provide a single objective measure for Chiari/SM

Definitions

Alzheimer's Disease - a progressive brain disease which causes memory loss, confusion, and dementia

beta amyloid - a protein that exists in the brain and has been shown to build-up into plaque deposits in people with Alzheimer's

cerebellar tonsils - portion of the cerebellum located at the bottom, so named because of their shape

cerebellum - part of the brain located at the bottom of the skull, near the opening to the spinal area; important for muscle control, movement, and balance

cerebrospinal fluid (CSF) - clear liquid in the brain and spinal cord, acts as a shock absorber

Chiari malformation - condition where the cerebellar tonsils are displaced out of the skull area into the spinal area, causing compression of brain tissue and disruption of CSF flow

compliance - a measure of how much a vessel changes in volume due to a change in pressure; dV/dP; the inverse of elastance

dura - tough, outer covering of the brain

flow - in fluid dynamics, how quickly a volume of fluid travels through a container or vessel

fluid dynamics - the quantitative study of how fluids behave under different conditions

hypothesis - a tentative theory about how something works; not yet supported by experimental facts

impedance - in fluid dynamics, a measure of how much a vessel restricts pulsatile flow

interstitial fluid - in the human body, fluid that exists between the cells, in the small spaces in organs and tissues

pressure - a measure of the amount of force applied to a given surface area

resistance - opposition to flow; in this case to steady-state fluid flow

sub-arachnoid space - space underneath the arachnoid, but above the actual brain and spinal tissue, which contains the cerebrospinal fluid

syringomyelia (SM) - neurological condition where a fluid filled cyst forms in the spinal cord

syrinx - fluid filled cyst in the spinal cord

tonsillar ectopia - descent of the cerebellar tonsils into the spinal area

According to Bateman, the importance of compliance and impedance extend beyond just Chiari and syringomyelia into other conditions as well. Alzheimer's, the progressive brain disease, is believed to be caused by a build-up of a certain protein, beta-amyloid, into plaque deposits in the brain. Bateman believes that as people age, their brain tissue becomes more rigid and thus, less compliant. This means that the interstitial brain fluid has a harder time draining out of the brain (along the space outside of blood vessels). The impedance to this natural draining of the interstitial brain fluid in turn results in the build-up of the protein in question. Interestingly, some Chiari doctors have commented that the dura tends to thicken and get stiff as we age, accounting for why children tend to recover more quickly from surgery. A thicker, stiffer dura implies less compliance as Bateman suggested.

Bateman's ideas are not completely new. Several researchers are beginning to focus on the relationship between compliance and dementia, and his theory on syrinx formation shares some similarities with a hypothesis Chiari & Syringomyelia News reported on earlier this year. Also, several of the Scientific Advisors to this publication are performing research on the importance of compliance and impedance in Chiari and syringomyelia. In fact, one of our advisors is publishing a paper on the subject next month in a major journal.

Is all this stuff about compliance and impedance important, or is it just ivory tower mumbo-jumbo? If it turns out that compliance and impedance are important in understanding Chiari and SM and can be related to clinical outcomes, it may be possible to develop a single objective test to evaluate people both before and after surgery; something that has so far proved elusive. It would also provide a means to evaluate different surgical techniques - such as scoring the dura rather than opening it - by seeing how much they increase compliance. Finally, a true understanding of what is occurring in the spinal system compromised by Chiari malformation will hopefully lead to new, and innovative, treatments.

Figure 1
Pulsatile & Steady-state Flow

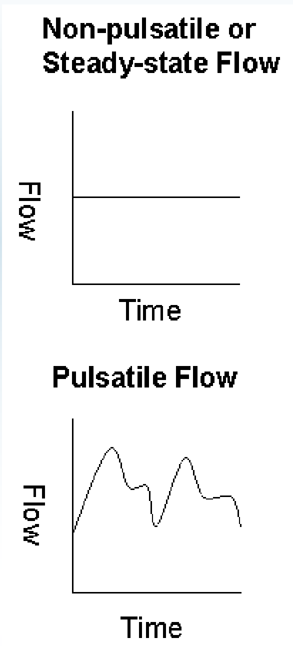
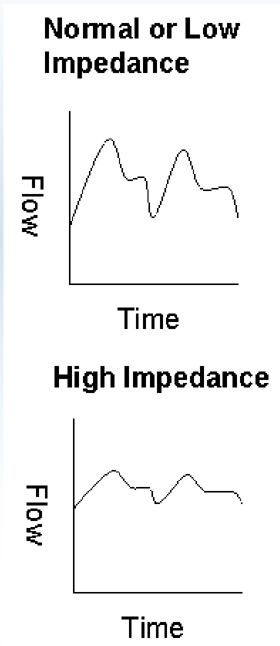


Figure 2
Effect of Impedance on Pulsatile Flow



- Resistance restricts, or decreases steady-state flow
- Resistance is related to the size of the vessel the fluid is flowing in - a larger diameter hose offers less resistance
- Impedance restricts pulsatile flow
- Impedance is related to the vessel's compliance, or it's ability to handle a changes in pressure
- When a vessel, or tube, has high impedance (low compliance) it is not able to respond to the pulses of fluid and restricts the pulsatile flow