

Progressive supranuclear palsy

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WHAT DID THE AUTHORS STUDY? In the article, “Tau forms in CSF as a reliable biomarker for progressive supranuclear palsy,” Dr. Borroni and her coauthors (*Neurology*® 2008;71:1796–1803) looked at specific medical tests that could help physicians accurately diagnose this illness. Progressive supranuclear palsy (PSP) is rare and has similarities to several other progressive neurologic disorders. Because of this, they looked at the results of these tests not only in people with PSP, but also in those who had the “similar” illnesses. In addition, the authors compared the results of the tests to test results of people who *did not have* progressive neurologic disease.

Dr. Borroni and coauthors carefully studied the tests results for 166 people. All had undergone a detailed history, physical examination, and neurologic examination. All were monitored for more than 2 years. The reason for this long period of monitoring is that the illnesses, especially when they begin, can look like something else. As the illness progresses and other symptoms develop, the diagnosis becomes more clear. By following this group for more than 2 years, Dr. Borroni minimized any errors in diagnosis.

Of the 166 people, 21 were diagnosed with PSP. One hundred twenty-five people had progressive neurologic conditions such as Parkinson disease and Alzheimer disease. There were also a few other illnesses. Twenty-seven patients acted as the “controls.” They were “normal.” This last group needs more explaining. The “controls” were a group of people who had an MRI and lumbar puncture for other reasons. For instance, they may have had a headache, and in the process of evaluating the headache, these tests were needed. Although not entirely “normal,” as this group had experienced a neurologic symptom (for example, headache), they did not have a progressive neurologic illness.

A subset of patients had a specialized MRI of the brain and brainstem. Dr. Borroni used a specialized kind of MRI technology called *voxel-based morphology* (VBM). Everyone is different on the outside; similarly, we have slight differences in our brains as well. VBM is one way to “eliminate” the differences between people, allowing for more accurate measurements. VBM technology is not used on the whole brain. Instead, it focuses on specific regions of the

brain. This is important in illnesses such as PSP, which primarily affects deep brain structures such as the brainstem.

Dr. Borroni also studied each person’s cerebrospinal fluid (CSF). She did this by carefully analyzing the kinds of proteins that were in the CSF. Because CSF surrounds the brain, components of CSF can give physicians important clues as to what is occurring within the brain itself. In certain neurologic illnesses, the CSF will contain a specific protein called *tau*. Dr. Borroni looked at two types of tau. She then calculated the ratio between the two tau subtypes. She analyzed each patient (for both types), and then compared the results between people with different neurologic illnesses.

WHAT DID THE AUTHORS FIND? The first discovery was that people with PSP had a specific ratio of tau proteins. The ratio was *lower* in people with PSP. This ratio was significantly different not only from the control group, but also was different from other types of progressive neurologic illnesses. Not only this, but as the illness worsened, the ratio became ever smaller. In other words, there was a correlation not only between the illness and a low tau ratio, but the worse the PSP was, the lower the ratio became.

Next, Dr. Borroni looked at the MRIs, focusing her attention on the VBM images. In patients with a low tau ratio, a significantly decreased amount of nerve cells was seen in the brainstem. This difference was not seen in other parts of the brain.

WHY IS THIS IMPORTANT? When a progressive neurologic illness begins, the kinds of problems that occur, such as memory problems, may not point to a specific diagnosis. Only later, as more symptoms develop, does the diagnosis become clearer. Studies like the one that Dr. Borroni has published show how medical testing can help. Testing of this kind can make diagnosis more accurate. In addition, it can give the physician a tool that allows him or her to make the diagnosis *earlier*. Although there is no known treatment for PSP today, this may change as research progresses. Earlier identification of illness may then lead to improved treatment.

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About progressive supranuclear palsy

WHAT IS PSP? Progressive supranuclear palsy (PSP) is a rare brain illness. It affects about 5 people in 100,000, which means that there are probably about 20,000 people in the United States that have PSP. It typically starts after age 60. It is *progressive*, which means that it worsens over time. The term *supranuclear* refers to the region of brain that PSP affects the most. *Palsy* simply means weakness, another effect caused by the illness.

WHAT CAUSES PSP? In the vast majority of people, the cause is unknown. Scientists are looking for environmental causes such as an exposure to certain toxins. Another possibility is that the illness might be caused by a virus that the person had when he or she was younger. Although the virus caused little or no problems at the time, it may have set a chain of events in motion that later resulted in PSP. In rare cases, the illness is genetic. For this reason, scientists are also looking for genes that either cause the illness or ones that might predispose someone to getting the illness. For instance, a person might need to have the gene *and also* be exposed to a specific toxin in order to develop PSP.

HOW DOES PSP AFFECT THE BRAIN? PSP can cause problems with movement and coordination, which translates into problems with balance and walking. Some of the symptoms of this, such as stiffness, resemble symptoms of Parkinson disease (PD). PSP causes problems with the movement of the eyes. When this happens, people feel that their vision is blurred, or they may experience double vision. As the illness worsens, depression and personality changes become more common. Memory can be affected, in a way that is nearly identical with Alzheimer disease (AD). In some people, swallowing becomes a problem, and a feeding tube, usually placed directly into the stomach, is needed.

The reason that PSP affects so many different brain functions has to do with the area of the brain that it affects the most: the brainstem. The brainstem is a small region of the brain, but it contains many different important structures. For instance, the control of the eyes requires careful input from a small number of nerve cells that live in the brainstem. For

eye movements to occur smoothly, these cells are in constant communication with each other and with other parts of the brain. When the brainstem starts having problems, it is easy to see how the eyes might be affected.

For the brain to do all of things that it needs to do, different brain areas have to be connected together. Of course, for the brain to direct the body's movements, it must have excellent connections with the muscles. The place where all of the connections go from the brain to the body is the brainstem. In short, an illness that affects the brainstem can affect the ability to perform smooth, graceful movements.

PSP IS PROGRESSIVE PSP starts out very slowly and gradually gets worse. Because everyone is different, the first signs of PSP differ among individuals. For instance, some people may have the eye movement problems first, while others have more difficulties with movement in the beginning. In some, the memory problems start first. Because of this, PSP may initially be diagnosed as something else, such as PD or AD. As the illness worsens, however, and other symptoms arise, the diagnosis of PS becomes much clearer.

WHAT MEDICAL TESTS ARE NEEDED? To some degree, the choice of medical tests depends on the specific situation. However, everyone with PSP will have had a physical and neurologic examination in their doctor's office. The physician carefully looks for any signs or symptoms of PSP. Often, the doctor will order an MRI of the brain (and brainstem). Sometimes the MRI will show changes in the brainstem, supporting the diagnosis of PSP; however, in many people, these changes are very subtle. Specialized MRIs, such as the one used in Dr. Borroni's paper, can help increase the chance of picking up on these abnormalities. However, the abnormalities on MRI in people with PSP can also be seen in other illnesses like PD and AD. Although the MRI can be very helpful, it does not make the diagnosis all by itself.

If memory is a problem, memory testing may be needed. Called *neuropsychological testing*, the memory "test" is actually a battery of tests which are designed

to assess many different areas of thinking, attention, and, of course, memory. Neuropsychological testing can identify certain patterns of brain *dysfunction*, not only helping to establish the diagnosis, but assisting in the selection of the best possible treatment(s).

WHAT IS THE TREATMENT FOR PSP? There is no known treatment for PSP at this time. Until one is available, doctors treat the symptoms of the illness. For instance, when a person has the movement problems that are similar to PD, he may respond to levodopa, a medicine that is often used to treat PD. There are medicines that can help improve the memory problems in AD. These can be used to help memory problems in PSP. Physical therapy can help to maintain strength and mobility. Often, a person with PSP will require a combination of therapies,

usually under the direction of a team of medical specialists.

RESEARCH Current research is aimed both at understanding PSP better, as in Dr. Borroni's paper, and at improving the treatment for PSP. These two aspects of research go hand-in-hand. As we understand an illness more fully, we can devise better and better ways of treating it. Because of the overlap between PSP and other progressive neurologic illnesses, research in one area may spill over into another. For instance, research in AD may help to unlock the key to understanding PSP.

FOR MORE INFORMATION

Society for Progressive Supranuclear Palsy
<http://www.psp.org/>

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