Posterior Cortical Atrophy

V. Pelak, MD
Professor of Neurology and Ophthalmology
University of Colorado School of Medicine

The terminology surrounding Posterior Cortical Atrophy or PCA can be difficult to understand. Often people are confused about what is meant by the terms PCA, the Visual Variant of Alzheimer's disease, dementia, Alzheimer's disease and other disease terminology. This document should help guide you to a better understanding of these terms and the diagnosis of PCA.

What Is Posterior Cortical Atrophy or PCA?

PCA is a condition of the brain that progressively worsens over time and affects areas in the brain that process visual information. The eyes are not involved or affected in PCA. Symptoms vary with the person, but the most common presentation at onset is simply having difficulty seeing despite a healthy eye examination. As PCA progresses, symptoms become more apparent and people with PCA experience difficulty reading, difficulty finding objects that are in plain view, problems with depth perception, trouble driving, or problems recognizing objects, images, or faces. Although PCA is not caused by one disease, for the majority of patients with PCA the cause is Alzheimer's disease. A person with PCA, however, does not usually experience a significant problem with memory at the onset of symptoms, or has only mild memory problems associated with more significant visual symptoms. It should be noted that some new memories rely on processing visual information. Therefore, PCA can contribute to problems remembering visual information because the brain did not properly process the visual information. There is currently no one test that is used to make the diagnosis of PCA. Instead complete eye and neurologic examinations are necessary. Basic laboratory tests and brain imaging are also important components of the evaluation and are necessary in order be certain there is no other cause or treatable condition resulting in the visual symptoms. Although PCA was named because of the distinctive atrophy of the cortical regions in the back of the brain, atrophy of the posterior regions of the cortex might not be prominent on an MRI at onset. The cortex is a special part of the brain that is a major part of the brain's "grey matter" and it is the convoluted or "wrinkled" part of the brain that we most often see in pictures or drawings of the brain. Visual field tests and standard cognitive and thinking tests of attention, memory, language, and executive functions are helpful in differentiating PCA from other problems. There is currently no disease-modifying treatment, but supportive measures and symptomatic therapies can help.

An autopsy can be performed at the time of death to determine the cause of PCA. The medical community has information from less than 75 such autopsies. In these

instances, where we can confirm the cause or causes of PCA by autopsy, the most common cause is Alzheimer's disease (approximately 75% of autopsies for PCA). In slightly more than 10%, the cause is a combination of Alzheimer's disease and Dementia with Lewy Bodies. Other causes include a combination of Alzheimer's disease and Dementia with Lewy Bodies or rare conditions such as one of the following: Corticobasal Degeneration, Creutzfeldt-Jakob Disease (a transmissible spongiform encephalopathy and it is also a type of prion disease). By clicking on the disorder, your browser will take you out of our webpage and to an information page about the disease on the National Institutes of Health website. In addition, some of these diseases are reviewed here as well.

In summary, PCA is a syndrome and not a disease. This means that it is a constellation of symptoms that can be caused by different diseases. As noted, the most common disease to cause PCA is Alzheimer's disease (approximately 75%), and some people with Alzheimer's disease causing PCA can also have Lewy Bodies contributing to their PCA syndrome (about 10%). In others, PCA is caused only by Lewy Bodies (approximately 5%). The remainder of the 10% is due to corticobasal degeneration, prion disease, or a combination of diseases.

Classification of PCA

We can classify the PCA syndrome using criteria set forth in 2017. The classification of PCA allows for communication using a common language and specific criteria. There are three levels of classification, as outlined here. Level one establishes the diagnosis of PCA, level two establishes whether there are symptoms and signs that meet diagnostic criteria for other disorders that are present with PCA, and level three establishes whether there are findings on tests (i.e. biomarkers) that provide evidence for a specific disease process in the brain. The levels are noted here.

Level I classification: *PCA syndrome*, which is a term used when specific clinical criteria are met.

Level II classification: *PCA-pure syndrome* versus *PCA- plus syndrome*, which are terms used as follows: *pure* indicates that a person has PCA syndrome (level I) and does NOT meet clinical criteria for diseases such as Alzheimer's disease (AD), Lewy Body Dementia (LBD), Corticobasal Degeneration (CBD), Prion disease, or other; *plus* indicates that a person has PCA syndrome (level I) and does meet clinical criteria for Alzheimer's disease, or Lewy Body Dementia, or Corticobasal Degeneration, or Prion disease, or other.

Level III classification: *PCA-AD* or *PCA-LBD* or *PCA-CBD* or *PCA-prion,* which are diagnostic terms that can be used when a person with PCA syndrome (level I) has biological markers of a specific disease such as Alzheimer's disease (i.e. markers of tau and amyloid), or Lewy Body Dementia, or Corticobasal Degeneration, or Prion disease. Currently, there are only conclusive biological marker tests available for Alzheimer's disease and Prion Disease.

Is the Visual Variant of Alzheimer's Disease the same thing as PCA?

The visual variant of Alzheimer's disease (or VVAD) is a term used to describe people with Alzheimer's disease who have prominent visual symptoms due to brain dysfunction from Alzheimer's disease. VVAD is a term that is slowly falling out of favor but is sometimes useful when a person has prominent visual symptoms and prominent memory symptoms simultaneously due to Alzheimer's disease. However, it is also true that PCA syndrome can precede the development of what one might refer to as the VVAD. Alternatively, people might be diagnosed with VVAD and have never had PCA. The major difference is that memory impairment and/or impairment in other areas of cognition occur equal to, or worse than, visual impairment in VVAD but not in PCA. However, it should be emphasized that there is no agreed upon criteria for VVAD but there is consensus criteria for PCA, which is discussed above.

What is Dementia?

This is a very general term that is used to indicate impaired abilities in memory, cognition, visuospatial functions, language, and/or thinking that do not allow one to function independently. PCA syndrome leads to dementia. Dementia can occur for many different reasons and be due to many different diseases including: Alzheimer's disease (the most common reason in the elderly), Lewy Body dementia, stroke(s), encephalitis, and others.

What is Alzheimer's disease?

This is the most common cause of age-related dementia. This is a disease of the brain that leads to dementia and progresses over time. The brain degenerates as cells of the brain die over time. Alzheimer's disease starts in the brain 20 or more years before symptoms. To make a definite diagnosis of Alzheimer's disease one must have markers of Alzheimer's brain disease on autopsy or in spinal fluid, where we look for abnormal accumulation of amyloid and tau proteins. Imaging for amyloid can be done with a PET-Amyloid scan. A brain scan by PET-FDG (i.e. glucose metabolic study) cannot reveal the cause as Alzheimer's disease. A PET-FDG brain scan is simply a study of the brain's metabolism and not of a specific disease. However, there are specific patterns that can point toward specific causes of cognitive impairment or dementia, but results of the scan cannot be used to diagnose the disease. There are no curative treatments for Alzheimer's disease, but supportive therapies and medications for Alzheimer's disease that have been proven effective.

What is Lewy Body Dementia (LBD)?

This is the second most common cause of age-related dementia. This is a disease of the brain that results in dementia. Just as in Alzheimer's disease, the brain degenerates as cells of the brain die over time. There is still much to learn about LBD,

but we do know that patients can develop symptoms of Parkinson's disease later in the course of disease. This is because Parkinson's disease and Lewy Body Dementia share an abnormal accumulation of a protein called alpha-synuclein. In fact, there is some data to show that LBD and Parkinson's disease are two different expressions of the same disease. To be certain, the abnormal alpha-synuclein protein looks the same under the microscope but accumulates in different regions of the brain for LBD compared to Parkinson's disease. Eventually symptoms from these disorders can overlap significantly. Of note, up to 60-80% of people with Lewy Bodies in their brains also have Alzheimer's disease in their brains. As with Alzheimer's disease, there are no curative treatments for LBD, but supportive therapies and medications have been shown to help symptoms.

What is Corticobasal degeneration (CBD)?

This is a more rare form of age-related dementia. This is a disease of the brain that results in dementia. Just as in Alzheimer's disease and Lewy Body Dementia, the brain degenerates as cells of the brain are lost over time. Within the brain there are changes in the neurons that are specific to corticobasal degeneration that are NOT found in Alzheimer's disease or Lewy Body Dementia. There are no curative treatments for CBD, but supportive care and some medications can help ease symptoms.

What is Prion Disease?

It is a rare disease of the brain that leads to more rapid deterioration and death than other diseases noted here. It is due to a protein that can be transmitted as an infectious agent, but is not transmittable in the way that a virus is transmittable. It requires exposure to brain tissue or spinal cord tissue or spinal fluid from someone with the disease. It can also come from instruments that have touched these tissues or fluids and then contaminate another person's brain or spinal fluid. There is currently no cure or treatment for prion disease and survival is typically less than 1-2 years after the development of the first symptom.

For more information about PCA and other diseases noted, see web links provided in the initial portion of this document and on the Colorado PCA support webpages.