Symptoms & Causes of PPA

What Are the Symptoms?

With primary progressive aphasia (PPA), the impairments in language appear gradually and get worse over time. In many instances, the person with PPA may be the first to notice that something is wrong and the changes in language may initially be attributed to stress or anxiety. Symptoms vary from one person to the next. The initial symptoms can include:

- Slowed speech
- Word-finding hesitations
- Sentences with abnormal word order in speech or emails
- Substitution of words (e.g., "table" instead of "chair")
- Using words that are mispronounced or incomprehensible
- Difficulty understanding what words mean
- Difficulty following a conversation despite normal hearing
- Forgetting the names of familiar objects
- Inability to think of names of people, even though the person is recognized
- New impairments in spelling

Scientists have proposed three "subtypes" or "variants" of PPA based on initial symptoms. However, each person with PPA is unique and may have symptoms that do not fit neatly into one subtype or may have features of more than one subtype.

PPA-G (Agrammatic/Nonfluent Subtype)

A problem with word-order and word-production

Speech is effortful and reduced in quantity.

Sentences become gradually shorter and words may be left out.

Word order may be abnormal, especially in writing or emails.

Words may be mispronounced or used in the reverse sense (e.g., "he" for "she" or "yes" for "no").

Understanding single words is preserved, but sentence comprehension may suffer if the sentences are long and grammatically complex.

PPA-S (Semantic Subtype)

A problem with word-understanding

The person may seem to have forgotten the names of familiar objects.

Single words are misunderstood, even of common words. When asked to bring an orange, for example, the person may appear puzzled and may ask what an “orange” means. However, when provided with an orange, the person will know that it is something that you can eat.

Speech is often fluent but somewhat empty of meaning. Filler words and phrases (e.g., "that thing over there") may be used more frequently.

PPA-L (Logopenic Subtype)

A problem with word-finding

Individuals have difficulty recalling the names of objects and/or thinking of words in conversation, but understand what those words mean.

Individuals may substitute a different word for the one they cannot find. They may use a simpler word or insert fillers such as "the thing that you use for it," "you know what I mean" or "whatchamacallit."

Speech may be fluent during causal small talk but breaks into mispronunciations and word-finding pauses when a more difficult or precise word needs to be used.

Individuals may have difficulty repeating phrases or sentences.

What Happens Over Time?

Because PPA is progressive, language ability continues to decline. Additionally, changes in non-language abilities (including memory, attention, judgment or changes in behavior and personality) may occur. Movement or swallowing may also become challenging for some individuals. The rate of decline is variable from person to person and unfolds over years. Scientists are working to understand why some people progress more rapidly than others.

What Causes PPA?

The symptoms of PPA occur when brain cells malfunction in language-related parts of the brain due to the accumulation of abnormal proteins. The underlying diseases causing PPA are called "neurodegenerative" because they cause gradually progressive brain cell death that cannot be attributed to other causes, such as head trauma, infection, stroke or cancer.

There are several types of neurodegeneration that can cause PPA. The three most commonly encountered types are:

Frontotemporal lobar degeneration with abnormal tau protein accumulation (FTLD-tau)

Frontotemporal lobar degeneration with abnormal TDP-43 accumulation (FTLD-TDP-43)

Alzheimer's disease (AD)

When abnormal proteins from AD or one of the forms of FTLD attack the language areas of the brain, PPA results. PPA is caused by AD in approximately 30 to 40 percent of cases and by one of the forms of FTLD in approximately 60 to 70 percent of cases.

The neuropathologic diagnosis of AD or one of the forms of FTLD can only be definitively determined at autopsy through examination of brain tissue with a microscope. However, scientists are working to identify biomarkers that can be used to make the diagnosis during life. Specialized brain scans using positron emission tomography (PET) and examination of cerebral spinal fluid (CSF), obtained through lumbar puncture, are two biomarkers currently being investigated to assist with determining the neuropathologic diagnosis. Scientists are working to identify additional reliable biomarkers.

"Is it PPA or is it AD?"

It can be both. The word "Alzheimer's" can be used in two different ways. The term "Alzheimer's disease dementia" (or "dementia of the Alzheimer-type") is used to designate a progressive loss of memory leading to a more generalized loss of all cognitive functions. The term "Alzheimer's disease" (as opposed to "Alzheimer's dementia") is used to designate the accumulation of two abnormal proteins in the brain, amyloid plaques and neurofibrillary tangles. Sometimes these abnormal proteins build up in language areas (instead of memory areas) of the brain, resulting in language impairments and thus the clinical diagnosis of PPA. So, while PPA patients don't have Alzheimer's dementia, 30 to 40 percent may have an atypical form of Alzheimer's disease. In this example, the individual would have a clinical diagnosis of PPA and their neuropathologic diagnosis would be Alzheimer's disease. This dual use of the word "Alzheimer's" is confusing, even for the specialist.

In the vast majority of patients with AD, the most prominent clinical symptom is a memory loss for recent events (amnesia) rather than an impairment of language (aphasia). PPA due to AD may be referred to as an "atypical" consequence of AD.

Is there a relationship between PPA subtype and neuropathologic diagnosis?

There is no one-to-one relationship between PPA subtype and underlying pathology. However, PPA-S (semantic variant) is most commonly associated with FTLD-TDP; PPA-G (agrammatic/nonfluent variant) is most commonly FTLD-tau; and PPA-L (logopenic variant) is most commonly associated with AD. These are only probabilities. Better biomarkers are needed to determine the neuropathologic diagnosis for each individual during life.

What role do genetics and other risk factors play?

In the vast majority of individuals, PPA is not genetic. However, in a small number of families, PPA can be caused by hereditary forms of FTLD. The most common gene implicated in these families is the progranulin gene (GRN). Other, less-common genes implicated in FTLD include the microtubule associated protein tau (MAPT) and chromosome 9 open reading frame 72 (C9ORF72).

The risk factors for PPA seem to be different than that of Alzheimer's disease dementia. The biggest genetic risk factor for Alzheimer's disease dementia is ApoE4. However, research evidence indicates that ApoE4 is not a risk factor for PPA caused by AD.

Personal history or family history of learning disability in a first-degree relative, especially dyslexia, has been reported as a risk factor for PPA but not for Alzheimer's disease dementia.

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