Behavioral Neurology Takes You on a Tour of the Brain

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Abstract

For years Behavioral Neurology studies of focal syndromes has depended on patients with stroke and tumor lesions. With the development of imaging tools such as voxel based morphometry degenerative brain disease has expanded anatomical related syndromes such as the primary progressive aphasias. This paper describes degenerative brain disease cases illustrating focal syndrome onset related to the anatomy of the initial and most severe degeneration. The paper will start in the frontal area describing a patient with behavioral variant frontotemporal dementia relating the published criteria and different pathologies to this syndrome. The paper then describes a patient with posterior cortical atrophy affecting the occipital and parietal lobes and pointing out that these patients have preserved anterograde memory and other clinical features with which the anatomy correlates. Alzheimer pathology is typical but the syndrome may also be caused by corticobasal syndrome. The third case is one with corticobasal degeneration affecting the parietal lobe which has published criteria and a myriad of pathologies that may cause this syndrome. The next two case illustrations will be semantic dementia from the left more than right temporal lobe and prosopagnosia affecting the right more than left temporal lobe. The paper will discuss the diagnostic criteria and typical pathology of these cases. The paper describes a patient with non-fluent primary progressive aphasia and demonstrates that Progranulin mutation patients may present this way. To round out the causes of primary progressive aphasia the paper will describe a case with logopenic aphasia. The published criteria and typical pathology will be added. Lastly the paper describes an Alzheimer patient that demonstrates different memory pathways with the patient having retained “know how” (procedural memory) but not “know what” (episodic memory) and the underlying pathological anatomy that causes this. In conclusion Behavioral Neurology syndromes have expanded with the study of degenerative dementia.

Key Words: Degenerative brain disease and Behavioral Neurology

Behavioral Neurology takes you on a tour of the brain
illustrated by focal onset degenerative cases

【Case 1】Frontotemporal dysfunction. Behavioral Variant Frontotemporal Dementia (bvFTD)

A 54-year-old right-handed surgeon had gradually progressive difficulties with hygiene, inappropriate laughter, bursts of anger, restricted insight and fixation on watching television. The patient had a complete change of personality for example he spent more than 10 hours per day watching television and remarkably was able to describe the shows he watched each hour and on which channel the programs were shown. This demonstrated his excellent memory and perseverative behavior. He has been forced to retire at age 51. He died 10 years later. His magnetic resonance imaging (MRI) showed mild bilateral frontal lobe atrophy, his fluorodeoxyglucose positron emission tomography scan (FDG PET) demonstrated hypometabolism in both frontal lobe. An autopsy was not

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performed.

A summary of the published criteria (Rascovsky et al., 2011) for bvFTD are:

**Possible bvFTD**
- Progressive deterioration of behavior/cognition
- Early behavioral disinhibition
- Early apathy
- Early loss of sympathy or empathy
- Early perseveration
- Neuropsychology profile executive spared memory

**Probable bvFTD**
- Probable is defined as possible plus functional decline and +ve imaging

**Definite**
- Definite is defined as pathological or genetic confirmation

The patient above clearly met the probable bvFTD criteria above.

The pathological causes of bvFTD include: TAR DNA Protein-43 (TDP-43), sub categories involving the tau protein including Corticobasal Degeneration (CBD), Pick's disease (PD) and rarely Alzheimer disease (AD) (Barker et al., 2002). Figure 1 illustrated the areas most affected in patients with bvFTD.

**Case 2  Occipitoparietal dysfunction : Posterior Cortical Atrophy**

A 51 year old woman complained that she had difficulty with vision and was referred to an ophthalmologist who examined her eyes and noted normal visual acuity. Her problem progressed to the point that she did not see a car coming towards her in the street and was nearly run over. Her husband had noted that she had difficulty wrapping the cord onto the vacuum cleaner handle. Despite her difficulties the patient retained her sense of humor and had good insight. Her degeneration slowly progressed and she died 14 years after onset and an autopsy

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![Figure 1](image-url)

This figure illustrated the areas most affected in Behavioral Variant Frontotemporal Dementia.
was completed. Figure 2 shows her T2 axial magnetic resonance scan.

The clinical picture in Posterior Cortical Atrophy (PCA) in our series (Tang-Wai et al., 2004) was:

1. Preserved insight 34/40
2. Complete or partial Balint Syndrome 38/40
3. Complete or partial Gertsmann syndrome 24/40
4. Visual field defect 19/40

The most common pathology was Alzheimer disease but compared to typical AD tangles were more frequent in inferior parietal lobe, Brodmann areas 17 and 18 but less frequent in superior temporal, subiculum and hippocampus CA1. This distribution correlates well with the clinical picture of visual loss, parietal dysfunction but relative preservation of memory and insight. Two of our cases had CBD pathology.

We have evaluated the PCA genetic associations from the reported late onset AD genetic associations and found that ApoE4 is associated and there is nominal association with CLU, BIN1 and ABCA7 (Carrasquillo et al., 2014)

**Case3** Parietal lobe dysfunction: Corticobasal syndrome

A 56-year-old right hand teacher with a master degree had a two year history of difficulty writing and slowly developed poor use of her right more than her left hand. She could no longer play the piano, do buttons and tie laces. On examination she had left right confusion, poor arithmetic abilities, dressing apraxia and limb apraxia. Her memory and speech were preserved. Her MRI showed mild left more than right parietal atrophy and her deoxyglucose positron emission tomography (PET) showed left more than right hypometabolism. The patient met criteria for probable corticobasal syndrome. These criteria are (Armstrong et al., 2013):

An asymmetric presentation of 2 of the following: a) limb rigidity or akinesia, b) limb dystonia, c) limb myoclonus plus 2 of: d) orobuccal or limb apraxia, e) cortical sensory deficit, f) alien limb phenomena.

![This MRI shows the typical MRI findings in patient with Posterior Cortical Atrophy.](image)
The clinical syndrome has an heterogeneous pathology. In the Mayo series we found of 13 case (Boeve et al., 1999):
Corticobasal degeneration (n=6), Alzheimer’s disease (n=2), Pick’s disease (n=1), Progressive supranuclear palsy (n=1), Creutzfeldt-Jacob disease (n=2), Dementia lacking distinctive pathology (n=1) This last case likely had TDP-43 pathology.

In contrast patients with the pathological findings of corticobasal degeneration may have the following clinical presentations (Armstrong et al., 2013): corticobasal syndrome, frontal behavioral-spatial syndrome, non-fluent agrammatic progressive aphasia and progressive supranuclear palsy syndrome.

**Case 4** Left temporal lobe dysfunction: Semantic dementia (SD)
An 83 year old practicing lawyer presented with the complaint that he had ‘lost the use of nouns but not verbs.” On the Boston naming test he could not name simple items like scissors, whistle and comb. Interestingly he could demonstrate the use of all these items. When shown the comb picture he could not name comb but when asked what he did with it he said he used it to comb his hair and then he was again asked what it was, he could not name it using comb as a noun.

The definition of SD (Gorno-Tempini et al., 2011) is poor confrontation naming and impaired single-word comprehension, explained by dissolution of semantic knowledge. There is no motor speech disorder or agrammatism.

**Case 5** Right temporal lobe dysfunction: Prosopagnosia and Semantic Dementia
A 75 year old right handed man had a two year history progressive difficulty recognizing faces and the naming objects. He enjoyed playing bridge and had little difficulty with short term memory and orientation. On examination he scored 27/30 on the MMSE, 10/20 on the first 20 items of the Boston Naming Test and 0/20 on recognizing the faces of very famous persons. His MRI is seen in figure 3.

Patients with the right more than left temporal lobe atrophy variant of SD often have prosopagnosia plus difficulty naming objects in pictures or being able to define an object when the word is spoken to them.

In Hodges autopsy series (Hodges and Patterson, 2007) of SD 14/20 had TDP-43 pathology and less commonly
Pick’s disease and 2/20 Alzheimer disease.

**Case 6** Parietotemporal junction: Primary progressive Aphasia, logopenic variant

A 66 year old right handed woman had a one year history of language difficulty. On exam the patient’s Mini-Mental Score was 28 of 30. She could not repeat “no ifs, ands or buts” and she struggled with naming a watch. On the Boston Naming Test she scored 20/25 on the first 25 items, without cues. She had difficulty repeating uncomplicated and complicated sentences. On naming the last 3 presidents and their wives’ first names, she scored 5/6.

This patient has the typical features of logopenic aphasia and that is an immediate memory difficulty with impaired sentence repetition. The deficits are thought to localize to the parietotemporal junction. The most common pathology found in patients with this syndrome is Alzheimer disease (Leyton et al., 2011).

**Case 7** Broca’s area: Progressive Non-Fluent Aphasia

A 65 year right handed man presented with slowly progressive language difficulty. His two sisters had the same syndrome and died with dementia. The patient first mixed up syllables, then had word finding problems and eventually could not say a full sentence. He was able to articulate well but had impaired naming, sentence repetition and comprehension. Interestingly, he functioned well and took care of their yard, helped his brother with carpentry and helped around the house. We reported him as having a hereditary primary progressive aphasia (Krefft et al., 2003) and later he was found to have a Progranulin mutation (Mesulam et al., 2007).

This patient had agrammatic non effortful speech. Often patients with effortful speech have tau as the underlying pathology for example cases with CBD may present this way. The second most common pathology is TDP-43 which was the underlying pathology in this patient who eventually came to autopsy. Imaging abnormalities may show atrophy of the left posterior frontoinsular area and or the supplementary motor area (Gorno-Tempini et al., 2011).

Figure 4

This MRI shows is of a patient with the clinical syndrome of logopenic aphasia and shows left more than right cortical atrophy.
Subcortical memory circuits. Memory underlying “knowing how” versus “knowing what.”

In 2001 a 71-year-old women complained of some memory difficulty and was diagnosed with Mild Cognitive Impairment but her MMSE was 29/30. By 2004 her MMSE was 27/30 and she still met criteria for MCI. In 2007 she declined and was diagnosed with Probable AD: MMSE 22/30. In 2009 her MMSE was 16/30 but she played 2 recitals monthly lasting 40 minutes including 9 pieces.

This interesting discrepancy of being able to play musical pieces (have preserved procedural memory) but not being able to learn the date of new information (anterograde memory) may occur in AD. This has been demonstrated in a study showing AD patients can learn mirror drawing but deny knowing the task each time they are trained on it (Eslinger and Damasio, 1986). In a careful study of the anatomical distribution of tangles in Alzheimer disease (Arnold et al., 1991) the primary cortices and the subcortical areas are usually not affected which is the anatomical basis for preserved procedural memory with impaired anterograde memory.

Conclusion

These cases illustrate how the study Behavioral Neurology in the setting of degenerative brain disease with the new imaging methods, genetic tools and pathological advances has demonstrated new syndromes. This has allowed neurologists to recognize these syndromes and the likely underlying pathology. When therapies against the underlying pathologies are found this clinical skill will become even more valuable.

References