Preferential Disruption of Auditory Word Representations in Primary Progressive Aphasia With the Neuropathology of FTLD-TDP Type A

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Abstract: Four patients with primary progressive aphasia displayed a greater deficit in understanding words they heard than words they read, and a further deficiency in naming objects orally rather than in writing. All four had frontotemporal lobar degeneration-transactive response DNA binding protein Type A neuropathology, three determined postmortem and one surmised on the basis of granulin gene (*GRN*) mutation. These features of language impairment are not characteristic of any currently recognized primary progressive aphasia variant. They can be operationalized as manifestations of dysfunction centered on a putative auditory word-form area located in the superior temporal gyrus of the left hemisphere. The small size of our sample makes the conclusions related to underlying pathology and auditory word-form area dysfunction tentative. Nonetheless, a deeper assessment of such patients may clarify the nature of pathways that link modality-specific word-form information to the associations that mediate their recognition as concepts. From a practical point of view, the identification of these features in patients with primary progressive aphasia should help in the design of therapeutic interventions where written communication modalities are promoted to circumvent some of the oral communication deficits.

Key Words: primary progressive aphasia, auditory word-form area, anomia, granulin

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AWFA = auditory word-form area. **FTLD** = frontotemporal lobar degeneration. **MRI** = magnetic resonance imaging. **PPA** = primary progressive aphasia. **STG** = superior temporal gyrus. **TDP** = transactive response DNA binding protein.

Primary progressive aphasia (PPA) is a neurodegenerative syndrome of progressive and initially isolated language impairment. PPA can be classified into agrammatic, logopenic, semantic, and mixed variants based on the status of a person's fluency, grammar, naming, repetition, and comprehension (Gorno-Tempini et al, 2011; Mesulam et al, 2014a). None of these variants is known to display selective impairments related to the route of stimulus input (auditory versus visual) or mode of response output (oral versus written). The current report was prompted by a patient with PPA (Patient 1) who showed relatively selective auditory and oral impairments of word comprehension and object naming. The selectivity of her impairment lent itself to a hodologic account centered on the disruption of a putative auditory word-form area (AWFA) located within the superior temporal gyrus (STG) of the left hemisphere.

Selectivity of language impairment is common in aphasia syndromes, including PPA. For example, patients with agrammatic PPA have greater difficulty naming verbs than nouns (Hillis et al, 2004), patients with logopenic PPA have longer word retrieval pauses for nouns than other parts of speech (Mack et al, 2015), and patients with semantic PPA have greater comprehension difficulties for words denoting living than nonliving objects (Bright et al, 2005).

Selectivity for sensory modality, however, has an uncertain status. The first six patients whose cases led to delineation of the PPA syndrome included one with characteristics of pure word deafness (Mesulam, 1982). In retrospect, the stability of her clinical course suggested that she should not have received a PPA diagnosis (Pinard et al, 2002). A literature search identified only three PPA cases with features of pure word deafness, where word comprehension (but not object recognition) was selectively impaired in the auditory but not visual modality (Iizuka et al, 2007; Kim et al, 2011; Otsuki et al, 1998). An auditory form of PPA is therefore exceedingly rare.

The selective impairment of auditory comprehension and oral naming in Patient 1 was unusual and did not fit into any known subtype of PPA. In the course of clinical investigations, Patient 1 was also found to carry a genetic mutation indicative of frontotemporal lobar degeneration–transactive response DNA binding protein (FTLD-TDP) Type A pathology. This finding triggered a retrospective review of our PPA autopsy series and led to the identification of three additional patients with similar clinical features. All three turned out to have FTLD-TDP Type A as the primary neuropathologic diagnosis. Type A accounts for only 10% of cases in our series of 110 consecutive PPA autopsies. We therefore felt that the conjunction of such a rare clinical pattern with a rare neuropathologic correlate of PPA deserved to be reported.

CASE REPORT

All four patients described here had comprehensive language evaluations during their diagnostic workup for PPA. Patient 1 had additional neurocognitive investigations that have been validated in prior studies of PPA. To normalize performance, we expressed patients' scores as percentages of correct responses. Imaging was done by standard magnetic resonance imaging (MRI) and metabolic positron emission tomography.

Case Descriptions

Patient 1

Patient 1 was a 60-year-old, right-handed woman at initial evaluation. She described a 3-year history of progressive difficulties in finding words, understanding instructions, and expressing her thoughts coherently. Because of these difficulties, she had been demoted from her managerial position. At home, she continued to perform household chores, maintain her checkbook, drive her car, and shop for groceries. She displayed adequate insight into her predicament. Her partner had not noticed changes in her personality. The history provided by her partner and the patient's cognitive neurology evaluation showed that her memory of recent events, recognition of familiar faces, visuospatial skills, and ability to use tools and objects were all preserved.

Patient 1's relatively isolated language impairment led to a diagnosis of PPA. More detailed language assessment showed that Patient 1's speech and writing were agrammatic and that she had impaired word comprehension—a combination that is characteristic of mixed PPA. Her speech was neither labored nor dysarthric but was mildly apraxic in multisyllabic words. Naming was severely impaired, as shown by a score of 15% on the Boston Naming Test (Goodglass et al, 2000). Performance on the Repetition subtest of the Western Aphasia Battery—Revised (Kertesz, 2006) was very low (13%). Fluency was low because of numerous word-finding hesitations. Surprisingly, Patient 1 could circumvent some of the word retrieval failures in speech by spelling aloud or writing at least the first few letters of the word she could not produce. Equally unusual was her ability to write the name of objects she could not name

orally. Furthermore, when figurines of animals, edibles, and tools were placed in front of her, she was less successful pointing to the object that corresponded to the noun she heard than to the noun she read (eg, cow, elephant). Although some of these findings are reminiscent of pure word deafness, the severe anomia and agrammatism were not consistent with that diagnosis.

Patient 1 passed a pure-tone audiometry screen from 250 Hz to 1000 Hz at 30 dB and from 100 Hz to 8000 Hz at 35 dB in the right ear; and from 250 Hz to 8000 Hz at 30 and 35 dB (with the exception of 6000 Hz at 35 dB) in the left ear. In a test that assesses phoneme discrimination (eg, *bin* and *pin*; *dime* and *dine*), she provided accurate answers for 82% of the items. Although we did not have normative values for this test, Patient 1's performance was interpreted as indicative of at most a mild impairment. Therefore, her profound deficits in auditory language tasks could not be attributed to underlying deficits of elementary auditory function or phoneme identification.

As shown in Table 1, additional tests were administered to quantify the selectivity of Patient 1's aphasia for the auditory modality. On the Peabody Picture Vocabulary Test, Fourth Edition (Dunn and Dunn, 2007), which is used to assess the ability to recognize words presented in the auditory modality, Patient 1's performance was very poor (47%). However, on the picture form of the Pyramids and Palm Trees Test (Howard and Patterson, 1992), which is used to assess nonverbal visual recognition of objects, her performance was high (90%). She also received a perfect score in matching 32 prerecorded environmental sounds (eg, rooster, trumpet, helicopter) delivered through headphones to pictures that depicted the source of the sound.

During a later videotaped testing session, Patient 1 was shown 17 objects. She named only 41% of the objects orally but was able to write (accurately or in easily recognizable form) the names of 77% of the objects she orally failed to name (Table 2). Patient 1 showed difficulty in

TABLE 1. Test Performance for Patient 1

Test	Score
PPVT–IV (test of auditory word recognition)	47%
PPTT (pictorial test of object recognition)	90%
BNT (object naming test)	15%
WAB–R (repetition test)	13%
Match 32 sounds to corresponding object picture	100%
Read a noun and touch one of 16 object pictures	92%
Reaction time for correct responses	4130 ± 394 msec*
Hear a noun and touch one of 16 object pictures	50%
Reaction time for correct responses	6291 ± 771 msec*

*Data shown as mean ± the standard error of the mean.
BNT = Boston Naming Test. **PPTT** = Pyramids and Palm Trees Test. **PPVT–IV** = Peabody Picture Vocabulary Test, Fourth Edition. **WAB–R** = Western Aphasia Battery—Revised.

TABLE 2. Word Recognition and Object Naming in Four Patients With Primary Progressive Aphasia

	Word Recognition Worse in Auditory Versus Visual Modality	Written Versus Oral Object Naming
Patient 1	Yes—pronounced	77% versus 41%
Patient 2	Yes—mild	43% versus 23%
Patient 3	No	82% versus 27%
Patient 4	No	88% versus 0%

reading words aloud in the Psycholinguistic Assessments of Language Processing in Aphasia (Kay et al, 1992), scoring 0 out of 10 for pseudowords, 3 out of 10 for regular words, and 0 out of 10 for exceptional words.

Patient 1 was also administered a task that required her to match a word she read or heard to one of 16 object pictures (Seckin et al, 2016). The object set consisted of 48 drawings that were evenly divided into four categories (animals, clothing, tools, and fruits/vegetables). On each trial, a noun cue from this set was presented in either auditory or written form followed by an array of 16 objects that included the target object and 15 foils. The interval between the cue and the appearance of the array of objects was 3 seconds. The task was to touch the object corresponding to the cue (object name); reaction times were recorded. The 48 items were split into two lists where the items in one list were given with an auditory cue first, and the items in the other list were given with a written cue first. Pictures were placed equidistantly apart along a 31.4 degrees by 24.2 degrees ellipse, with each picture subtending 3.4 degrees of visual angle, allowing foveal resolution with corrected visual acuity of at least 20/25. The corresponding nouns were balanced for lexical frequency, number of phonemes, and phonological neighborhood density (Balota and Yap, 2007).

Patient 1's accuracy in this task was 92% for visual presentation of the word and 50% for auditory presentation of the word, which is a significant difference at $P < 0.001$ (McNemar chi-square with Yates' correction [$df = 1$, N = 96] = 16.4). When all correct responses were considered, her mean reaction times and standard error of the mean in response to auditory and visual words was 6291 ± 771 msec (N = 24) and 4130 ± 394 msec (N = 44), respectively. For statistical comparisons, we included only items that were correctly responded to in both modalities (N = 24). Among these items, Patient 1's median reaction times were 3146 msec (first quartile: 2537 msec, third quartile: 4554 msec) for the visual presentation and 5904 msec (first quartile: 3040 msec, third quartile: 8465 msec) for the auditory presentation. The correct auditory reaction times were significantly slower (Wilcoxon signed rank test, W[23] = 75; $P < 0.05$), indicating that her level of certainty even for correct choices was less robust when linking an auditory rather than a visual word to its given cue.

Patient 1's MRI showed extensive but asymmetric atrophy in the left hemisphere, encompassing the inferior frontal gyrus and inferior parietal lobule as well as all parts of the left temporal cortex, including the STG and anterior temporal lobe. As shown in Figure 1A, Heschl's

gyrus (primary auditory cortex, A1) appeared relatively preserved, whereas the immediately adjacent lateral STG (auditory association cortex, AA) was severely atrophied. Patient 1 reported that her sister had a somewhat similar condition of progressive impairment of word finding. However, the sister was not available for testing.

Genotyping was done, and Patient 1 was found to have a disease-causing mutation in the *GRN* gene, which results in premature protein termination (p.Gln130Serfs*125). Such mutations are associated with the neuropathology of FTLD-TDP Type A (Mackenzie et al, 2010).
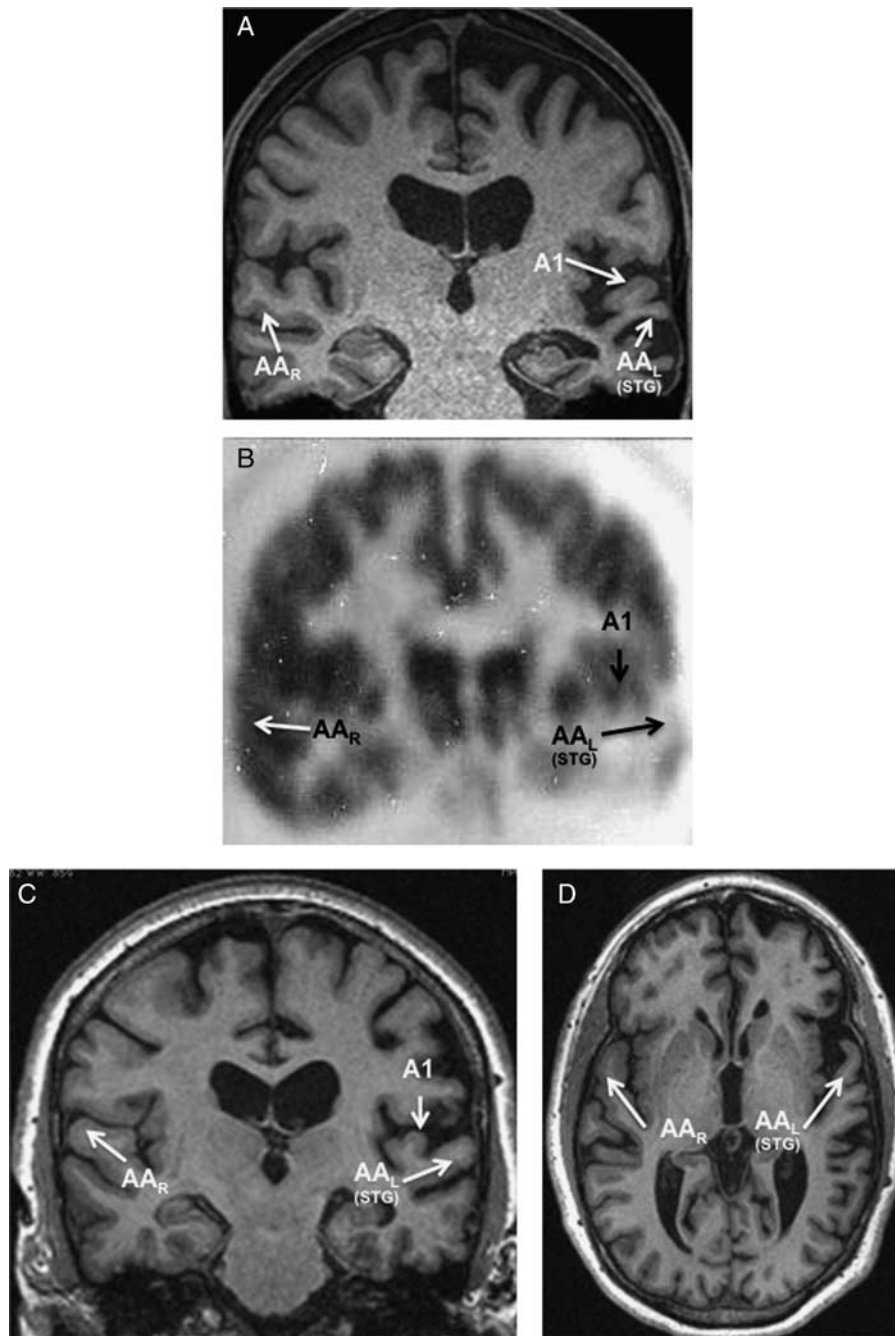
Patient 2

Patient 2 was a right-handed man who first noticed word-finding difficulties at the age of 55. Although he had to quit work because of his communication problems, he maintained his customary activities, including highly complex hobbies such as piloting his own airplane. At his initial examination 3 years later (at age 58), language was the only area of cognitive impairment. For example, Patient 2's speech had many word-finding pauses and circumlocution. This circumlocution made it difficult to assess the grammatical structure of his speech. There were no motor speech impairments. Comprehension of sentences based on familiar words he could understand was preserved in the auditory and visual modalities except for statements that were syntactically complex (eg, passive voice sentence construction). Single-word comprehension was at least partially preserved (see below). Confrontation naming and sentence repetition were severely impaired. His examination most closely fit the pattern of logopenic PPA.

When asked to name an object, Patient 2 would frequently take his pen out, grab a piece of paper, and write the name of the object while saying "That's just like it, just like it." In the vast majority of cases, the noun he wrote was accurate (eg, goose, turtle, button). Performance on the Boston Naming Test was 23% for oral responses and 43% for written responses (Table 2). The rare single-word comprehension failures were also more pronounced in the auditory modality. In a test of synonym judgment, for example, Patient 2's performance was 90% for visual words and 60% for auditory words.

When presented with geometric shapes, Patient 2 failed to orally name the cube, triangle, and rectangle and also failed to point to the correct shape when he heard the corresponding word, indicating an auditory recognition failure for the noun. Nonetheless, he could correctly write the names of the shapes, showing that the word retrieval and recognition problems were selective for the auditory modality.

Patient 2 passed a bilateral pure-tone screen at 35 dB except at 4000 Hz in the right ear, where a threshold of 55 dB was recorded.

The patient's MRI showed asymmetric atrophy of the left inferior parietal lobule and left temporal lobe, mostly the STG. Metabolic positron emission tomography showed relatively preserved metabolism in Heschl's gyrus (A1) but severe hypometabolism in the adjacent auditory association cortex of the left STG (Figure 1B). Family

FIGURE 1. Available imaging results. Magnetic resonance imaging of Patient 1 (**A**); metabolic positron emission tomography of Patient 2 (**B**); magnetic resonance imaging of Patient 3 (**C**, **D**). **A1** = primary auditory cortex (Heschl's gyrus). **AA** = auditory association cortex. **L** = left hemisphere. **R** = right hemisphere. **STG** = superior temporal gyrus.

history indicated that Patient 2's mother had been diagnosed with dementia at the age of 50. Postmortem examination revealed FTLD-TDP of Type A. Genetic testing showed a *GRN* mutation (p.Ala237Thrfs*6).

Patient 3

Patient 3 was a right-handed woman who noted progressive word-finding difficulties in speech and writing at the age of 55. Her initial examination 2 years later (at age 57) indicated that her daily living activities and other cognitive and behavioral domains were relatively preserved, although her verbal output was sparse (nine words per minute), halting, labored, and agrammatic. Her repetition of phrases and sentences was also impaired. She could recite the months of the year in 20 seconds, which is slow but not as slow as her spontaneous speech. The

difference between her spontaneous versus ordered word output suggested that the low fluency in her narrative was driven to a large extent by word-finding difficulties rather than speech impairment.

Patient 3 had no auditory or visual word comprehension deficit, as determined by a Peabody Picture Vocabulary Test, Fourth Edition score of 89% and a score of 100% in a test where she was asked to match each of 20 written words to one of 20 corresponding object pictures (Mesulam et al, 2013). She received a diagnosis of agrammatic PPA. In the traditional administration of the Boston Naming Test, where she was allowed up to 20 seconds to respond verbally, she scored very low (27%). However, when allowed to write the names (and also allowed up to 20 seconds to respond), her score increased to 82%.

Patient 3's MRI showed asymmetric atrophy. Heschl's gyrus was relatively preserved compared to the asymmetrical atrophy of the left STG, superior temporal sulcus, and middle temporal gyrus (Figure 1C). The posterior parietal cortex and inferior frontal gyrus also showed atrophy. Patient 3 had a brother with early onset dementia who also displayed unspecified language problems. The brother had never been tested cognitively. Eventual autopsy of Patient 3 and her brother revealed that both had FTLD-TDP Type A pathology. The *GRN*, *TDP-43*, and *C9orf72* genes, each of which can be associated with genetic forms of FTLD-TDP, had no disease-causing mutations. Investigations are continuing to identify a potential genetic cause.

Patient 4

Patient 4 was a right-handed woman who noticed difficulty finding and producing words at the age of 68. She was tested 2 years later and was found to have labored and hesitant speech with paraphasias and difficulty pronouncing multisyllabic words. Repetition was severely impaired. Her written language was more fluent but agrammatic. Auditory and reading comprehension did not show significant impairment, and neuropsychological evaluation found other cognitive domains to be relatively spared. Daily living activities that did not depend on language were also similarly spared. Based on this profile, a diagnosis of agrammatic PPA was made.

Patient 4's speech was deemed intelligible for phrase-length responses. Nonetheless, she was unable to name any of the Boston Naming Test pictures orally, but she successfully wrote the names of 88% of the items. A clinical MRI was reported unremarkable; the metabolic positron emission tomography report indicated areas of hypometabolism in the left parietal and superior temporal lobes. The scans were not available for further examination. There was no family history of similar condition. The postmortem examination revealed FTLD-TDP Type A as the principal diagnosis.

DISCUSSION

Patient 1 had the most systematic assessment. She displayed two dissociations, one at the input stage (auditory versus visual) and the second at the output stage (oral versus written). With respect to input, her comprehension was better for words she read than words she heard. With respect to output, naming was less impaired when she was allowed to spell or write the word than when she had to speak it. These dissociations could not be attributed to hearing loss, phoneme discrimination problems, or motor speech impediments.

Patient 1's performance in the 16-item word-picture matching experiment was particularly informative. As expected, accuracy was much higher when the word was presented in the visual modality. An even more interesting difference emerged in reaction times for targets where she correctly matched the word to the picture. The reaction times were slower when she heard the word than when she read the word. Thus, even when she was able to recognize the word accurately, the process was less robust when the word was accessed through the auditory modality. This dissociation was specific to the language domain because her recognition of auditory and visual objects was preserved.

As shown in Figure 2, these modality-based dissociations can be depicted diagrammatically as consequences of information processing bottlenecks along routes that link unimodal sensory areas to transmodal cortices of the language network. The areas and connections in Figure 2 reflect idealized information flow blueprints (or circuit boards) rather than discrete anatomical entities. The anatomical terms in the figure correspond to some of the locations where areas with analogous functionalities have been reported. The literature on each of the functional areas depicted in Figure 2 is vast (Mesulam, 1998). In this article, we cite only representative works to support the plausibility of this circuitry but do not discuss the range of opinions related to the nature of these areas and their interactions.

According to the diagram in Figure 2, Patient 1's pattern of impairment can be hypothetically accounted for by the dysfunction of an AWFA that is situated at the confluence of pathways mediating naming, word recognition (comprehension), and repetition. The AWFA is synaptically downstream from neurons that are sensitive to word-like but meaningless auditory patterns (eg, distorted backward speech) and responds selectively to word-like patterns that are also recognized as plausible words in the speaker's language (Creutzfeldt et al, 1989). Evidence from lesion and recording studies support the presence of such an AWFA within the mid regions of the left STG (DeWitt and Rauschecker, 2016). This area (a) receives input from more posterior areas that are selectively responsive to phonemes (pathway 1), (b) is selectively tuned to auditory patterns with familiar word-like properties, and (c) projects to transmodal areas of the anterior temporal lobe (pathway 2). Through these transmodal nodes, auditory word-forms can become linked to the distributed associations that collectively encode their meaning (Mesulam, 1998).

The transmodal associations include the linkage of the auditory word-form to the visual representation of the object it denotes (pathway 3). Areas specialized for encoding objects in the form of visual percepts have been located in the posterior fusiform and lateral occipitotemporal cortex
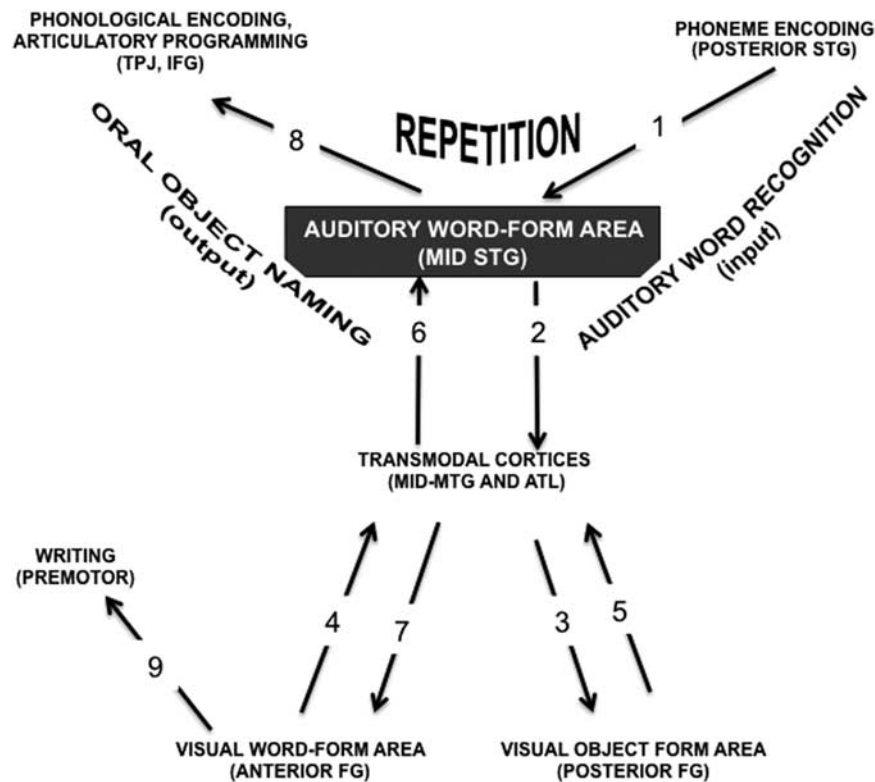
FIGURE 2. Information flow diagram depicting the circuitry that could underlie the selective language impairments in the patients described here. The anatomical sites are conceptual and refer to the locations where such functionalities have been reported in the literature. The identity of the pathways indicated by arrows remains to be determined. Although additional functional nodes (eg, the auditory equivalent of the visual object form area) could have been added to this diagram, we left them out to emphasize the circuitry underlying the major clinical deficits. **ATL** = anterior temporal lobe. **FG** = fusiform gyrus. **IFG** = inferior frontal gyrus. **MTG** = middle temporal gyrus. **STG** = superior temporal gyrus. **TPJ** = temporoparietal junction.

(Haxby et al, 2001). Pathways 1, 2, and 3 would collectively mediate the recognition of an auditory word as assessed by word-picture matching tasks that Patient 1 could not perform with any degree of efficiency. Her deficit in these tasks cannot be attributed to impairment of the visual object area because her nonverbal object recognition skills remained intact. Nor could the deficit be attributed to a primary impairment of transmodal cortices because such a lesion would have caused equally severe impairments in recognizing auditory and written words, a pattern that is characteristic of semantic PPA. A primary defect along pathway 1 can be excluded because of her relatively successful performance in basic auditory tasks. In fact, a defect confined to pathway 1 and its origins would have caused the different syndrome of pure word deafness in which phoneme identification is impaired but confrontation naming is intact (Coslett et al, 1984). Within the context of the information flow diagram depicted in Figure 2, Patient 1's auditory word recognition impairment implies a dysfunction centered within the AWFA and its output through pathway 2.

Compared to her impaired auditory word recognition, Patient 1's visual word recognition was better preserved. Preservation of this function can be attributed to the integrity of a visual word-form area that is known to exist in the fusiform gyrus (Nobre et al, 1994), which communicates with visual

object-form areas via the transmodal cortex of the temporal lobe (pathways 4 and 3). Although direct connectivity between the visual object-form and word-form areas almost certainly exists, it would not be expected to sustain the associative elaboration required for word recognition without the obligatory mediation of transmodal areas (Mesulam, 1998).

In the course of object naming, a visual object form is presumably conveyed to transmodal nodes (via pathway 5) that activate the corresponding multimodal associations of the object, including its lexical label (lemma) in oral (via pathway 6) and orthographic (via pathway 7) form. Oral naming was selectively impaired in Patient 1 presumably because the process depends on an AWFA as an obligatory gate along pathways that link the visual object percept to its orally articulated name (pathways 5, 6, and 8). In contrast, writing the name requires pathways 5, 7, and 9, which do not include or cross the AWFA. The impairment of oral naming cannot be attributed to a failure of phonological or articulatory encoding (pathway 8) because Patient 1 had no motor speech impairment. The proposed AWFA dysfunction would also account for her severe repetition impairment by interrupting the linkage between pathway 1 (hearing words) and pathway 8 (articulating words) and perhaps also by undermining the auditory working memory span. The AWFA depicted

in Figure 2 could conceivably encompass more than one subregion, each preferentially related to repetition, naming (output), and comprehension (input).

The dissociation at the input stage (auditory versus visual word comprehension) was seen in only one other patient (Patient 2), and even then to a lesser extent than in Patient 1 (Table 2). This probably reflects the method of testing where comprehension was assessed by word-picture verification, a process that may be computationally easier and therefore less sensitive to AWFA dysfunction than the naming task, which requires both retrieval and production of the relevant word.

All four patients shared the feature of being more impaired in oral than written naming. All four also had poor language repetition. All patients, therefore, had a central deficit in at least part of the putative functionality of the AWFA. The common site of atrophy in the auditory association cortex of the STG is in keeping with this conclusion. However, STG atrophy is very common in people with PPA, including other patients we have seen with TDP Type A, but it does not generally cause the selective impairments of the four patients described here. The precise anatomical bases of the auditory and oral features in the aphasias of our patients therefore remain unexplained and will require more sophisticated imaging studies based on functional connectivity and diffusion tensor imaging.

In the scans available for inspection (Patients 1, 2, and 3), atrophy could also be identified in additional temporal, frontal, and parietal cortices. In the two patients with agrammatism (Patients 1 and 3) atrophy in the inferior frontal gyrus encompassing Broca's area was observed; this was not observed in Patient 2. Furthermore, Patient 1, who had the most pronounced comprehension impairment, had the most severe atrophy of the anterior temporal lobe, which is a region that is known to be critical for word comprehension.

An unexpected finding was the presence of FTLD-TDP as the primary neuropathologic diagnosis in all four patients. The neuropathologic associations of PPA are heterogeneous. The most common include Alzheimer disease, FTLD with tauopathy, and FTLD with TDP-43 proteinopathy (FTLD-TDP) (Mesulam et al, 2014b). FTLD-TDP is classified into types A through D based on the morphology and distribution of abnormal TDP-43 inclusions (Mackenzie et al, 2010, 2011). Types A and C are the most relevant to PPA (Mesulam et al, 2014b). Type C is almost never caused by a genetic mutation and frequently gives rise to anterior temporal lobe atrophy and semantic PPA (Mackenzie et al, 2006; Mesulam et al, 2017). Type A can be genetic (associated with *GRN* mutations) or sporadic and can give rise to frontotemporal dementia, PPA, or even amnestic dementia (Baker et al, 2006; van Swieten and Heutink, 2008). The clinical phenotype (frontotemporal dementia versus PPA) is determined by the anatomical distribution of cortical atrophy and cellular pathology (Kim et al, 2016; Rohrer et al, 2010).

Of 110 consecutive PPA autopsies in our brain bank, only 11 (10%) have the pathology of FTLD-TDP Type A, with clinical pictures of agrammatic, logopenic, and mixed PPA without a clear pattern of selectivity (Mesulam et al, 2014b). Based on her *GRN* mutation, Patient 1 is the 12th

such case. The presence of agrammatism in three of the patients in this report may reflect the known association of Type A pathology with atrophy in the dorsolateral frontal cortex, including the inferior frontal gyrus (Rohrer et al, 2010). Although FTLD-TDP Type A is a relatively uncommon correlate of our PPA cases, this report shows that one-third of such cases in our brain bank display the rare auditory/oral language impairments described here. This association of a rare clinical syndrome with an infrequent pathology raises the possibility of a preferential (but not obligatory) relationship between FTLD-TDP Type A and auditory/oral language impairments in people with PPA.

One purpose of this report is to promote the identification of additional cases with these features so that the generality of this clinicopathologic correlation can be tested. Even if additional cases fail to support this association, the investigation of patients with these features should advance our understanding of the language network and also help to personalize treatment approaches aimed at circumventing the preferential auditory and oral impairments.

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