Full title:

Speech and language therapy approaches to managing primary progressive aphasia

Short title:

SLT in PPA

Authors:

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Abstract
The term primary progressive aphasia (PPA) describes a group of neurodegenerative disorders with predominant speech and language dysfunction as their main feature. Three main variants have been described – the semantic variant (svPPA), the nonfluent or agrammatic variant (nfvPPA), and the logopenic variant (lvPPA) – each with specific linguistic deficits and different neuroanatomical involvement. There are currently no curative treatments for PPA nor any symptomatic pharmacological therapies. However, there are a number of impairment-based interventions and compensatory strategies that have been developed by speech and language therapists (SLTs) for use in the clinic. Unfortunately, multiple barriers still need to be overcome to improve access to care for people with PPA, including increased awareness amongst referring clinicians, improved training of SLTs, and the development of evidence-based guidelines for therapeutic interventions. This review highlights this inequity and the reasons why neurologists should make a referral to an SLT for individuals with PPA.
Introduction

Progressive neurodegenerative disorders of speech and language dysfunction have been reported since the late nineteenth century. However it was only in the last quarter of the twentieth century that they were codified and fully described as the primary progressive aphasias (PPA) (1-3). These were initially felt to fall mainly within the frontotemporal dementia (FTD) spectrum but evidence from post mortem (and more recently amyloid PET and CSF) studies have shown that a proportion of cases have underlying Alzheimer’s disease pathology (4).

The present diagnostic criteria describe three subtypes of PPA, the semantic (svPPA), nonfluent or agrammatic (nfvPPA), and logopenic (lvPPA) variants (3). Whilst the majority of individuals with PPA presenting with primary speech or language dysfunction fit within these groups, a substantial minority of people do not. This unclassified, or not otherwise specified (PPA-NOS), group include those with very early clinical features not yet fulfilling diagnostic criteria, and those with a mixed picture of symptoms and signs (5).

There is currently no curative treatment for PPA, and the disease progresses inexorably over time. Symptomatic pharmacological therapies have also not shown any evidence of effectiveness and many clinicians therefore tend to be nihilistic about treating people with PPA. In fact, speech and language therapists (SLTs) across the world have worked for many years on tailored programmes for such people with PPA, and multiple speech and language therapeutic interventions have emerged (6,7). This review brings together current approaches to management of PPA,
highlighting the barriers to access to a specialist SLT, and provides suggestions for future priorities in developing better care.

**Clinical features of PPA**

PPA is a clinical diagnosis, made with the support of neuroimaging, usually in the form of either magnetic resonance imaging (MRI) or positron emission tomography (PET) (Figures 1 and 2; Table 1). The overarching PPA diagnosis is usually relatively clear as it requires the presence of a progressive disorder where speech and/or language dysfunction is the predominant symptom (3). In our experience, this is easier for nfvPPA and lvPPA compared with svPPA which can occasionally be misdiagnosed as Alzheimer’s disease or another form of dementia when word-finding complaints are mistaken for ‘memory problems’. Usually the more complex issue is the diagnosis of a specific PPA variant: firstly, it can sometimes be difficult to distinguish between the subtypes, particularly early on in the illness (and conversely, very late in the illness), and, secondly, as mentioned above, some individuals do not neatly fit into one of the three diagnostic groups. Figure 1 provides an overview of a relatively simple diagnostic algorithm for the PPA variants (see Marshall et al, 2018 (8) for more details) and Table 1 a more detailed description of the clinical features found on examination. The classical neuroimaging features of the PPA variants are shown in Figure 2.

Importantly from an SLT perspective, individuals with PPA may develop a motor disorder as the disease progresses. This is most commonly in those with nfvPPA, and may be either a non-specific hemiparkinsonian syndrome or a syndrome fitting more clearly into the pattern of
progressive supranuclear palsy or a corticobasal syndrome. Consequently, some individuals also
develop an associated dysarthria, and, over time, dysphagia.

PPA is pathologically and genetically heterogeneous (Figure 3). In most studies the majority of
cases of svPPA are associated with neuronal inclusions containing the TDP-43 protein, whilst
nfvPPA is usually associated with tau inclusions. LvPPA has been shown to be most commonly
an atypical form of Alzheimer’s disease, with amyloid plaques and neurofibrillary tangles seen
at postmortem. Each of the variants is generally sporadic in nature but a small proportion of
nfvPPA cases (probably less than 5%), as well as a number of individuals with PPA-NOS, are
genetic, typically caused by mutations in the progranulin gene. Appropriate genetic counselling
for these individuals and their families is important.

SLT interventions for people with PPA and their families

a) Impairment-based approaches

i) Word retrieval interventions

A number of studies have demonstrated that word retrieval interventions can be helpful for
people with PPA (9,10): a systematic review of 39 studies suggested that both semantic and
phonologically-based treatments, and in some cases combinations of both, demonstrate
immediate positive gains for people with PPA (9). It is less clear how generalisable the gains are,
and how long those gains are maintained (11). A recent systematic review examined those
questions in the context of semantic word retrieval therapies across the PPA subtypes (12):
generalisation was more likely in nfvPPA and lvPPA, with maintenance of gains demonstrated across all subtypes over a short time period, although degrading quickly without ongoing practice. Targeting functional, individually-tailored training sets, with pictures of participants’ own items, in both daily sessions with the clinician and home practice, as well as ongoing practice after the end of the formal treatment period, have all been found to promote relearning and maintenance (11) Ongoing research aims to identify additional components to word learning interventions that will facilitate generalisation to functional communication e.g. whether the provision of a verb or noun facilitates successful sentence production, and whether supplementing spoken word retrieval treatment with written naming is helpful. Figure 4 provides an example of how word retrieval interventions work using Repetition and Reading in the Presence of a Picture (13).

ii) Script training and other approaches to improving fluency

Few studies have implemented interventions to improve fluency in nfvPPA (14-19) and, among those, only two have addressed the core symptoms of agrammatism (14) and apraxia of speech (18). Schneider and colleagues examined a treatment for verb production in a single case with nfvPPA (14). They observed gains for treated verb tenses as well as generalized improvement on untrained verbs. Henry and colleagues implemented an oral reading treatment for apraxia of speech (18), observing generalized improvement in speech production at post-treatment, as well as relative stability in speech production over the year following treatment.
Whilst these initial small studies document positive outcomes, there is a need for more research investigating interventions tailored to the specific linguistic and motoric deficits observed in nfvPPA. A new study has attempted to address this need by implementing a script training approach, designed to improve speech production and fluency in nfvPPA, documentating not only immediate response to treatment, but also long-term outcomes up to one year post-treatment (19). Script training is an established intervention technique developed in stroke aphasia/apraxia and involves repeated rehearsal, with the goal of improving automisation of production and, in turn, intelligibility and grammaticality of output. Findings so far in nfvPPA have revealed significant improvement in accurate production of scripted content as well as improved overall intelligibility and grammaticality for trained topics post-treatment. Intelligibility also improved for untrained topics and gains in accurate production of trained scripts were maintained up to one year post-treatment. This work confirms that treatment targeting the core deficits of agrammatism and motor speech is capable of conferring significant and lasting benefit to individuals with nfvPPA.

Figure 4 provides an example of such a script.

b) Compensatory-based approaches

There is limited research to date on functional communication focused interventions for people with PPA (20). The studies that have focused on such interventions have tended to examine either communication skills training (21-23) or Augmentative and Alternative Communication (AAC) development or use (24-29).
In contrast to the lack of research, many specialist SLTs report prioritising communication skills training in their management approaches with people with PPA above more impairment-based interventions in actual day-to-day clinical practice (30,31). Taking its evidence base from the post-stroke aphasia literature, this approach targets everyday use of conversation between a person with PPA and a family member or carer, and is underpinned by an assessment of strategies that facilitate communication (e.g. gesture) and those that act as a barrier (e.g. interruptions or abrupt topic changes) (32). A recent study demonstrated that the use of facilitative behaviours by communication partners enhanced successful conversation in svPPA (33), and there is currently work underway piloting a randomised controlled trial of a freely available internet based resource (Better Conversations with PPA) to support SLTs to deliver communication training to people with PPA and their families (34).

Assistive Augmentative Communication (AAC) devices that employ both high technology (such as smart phones) and low technology (such as communication books) have been shown to be useful in supporting activities of daily living, such as shopping (23, 24) and cooking tasks (25; see figure 4), and conversations with trained conversation partners (6, 28, 29). Whilst communication books can often be quite simple reminders of everyday activities, a more detailed ‘life story book’, may help to facilitate improved emotional interactions between individuals with PPA and their partners (35). Harnessing technology to meet the complex communication needs of individuals with PPA provides opportunities beyond compensatory strategies. Technology could potentially be utilized in other ways including the provision of speech-language treatment via a web-based
platform (e.g. the Communication Bridge telemedicine platform) (36,37) and utilizing technology for leisure activities (e.g. playing Solitaire online, reading a book on Kindle etc.).

c) Group education and support

Group education and support, tailored to the needs of people with PPA and their family members, can provide opportunities to practice and problem solve communication strategies with other communication partners (38). Research shows that people with PPA and their families feel valued and more confident after attending these groups (38,39). Providing information about progression of their symptoms within a group environment can provide peer support about future challenges (38). Additionally, focusing on both language and non-language based activities can enable interaction in a group setting as the person’s communication declines (39,40). Table 2 provides a list PPA support groups across the UK, the US and Australia.

d) Therapeutic models – heading to a person-centred approach

A number of different models have been proposed as frameworks for structuring treatment interventions for PPA. A “staging” approach offers impairment-based interventions (with a focus on remediation and rehabilitation) to people in the early stages of PPA and then compensatory strategies (with the goal to develop strategies to facilitate completion of a particular task) provided only after restoration has failed and language skills have been lost. However, such a model may be at risk of promoting generic, one-size-fits-all solutions, which do not address the complex biopsychosocial impact that PPA has on the individual and their family (41). In a person-centred care approach on the other hand, the individual proactively informs the decisions being
made about care in dynamic interactions with the clinician. Models consistent with this approach include the Life Participation Approach for Aphasia (LPAA) (42) and the CARE Pathway model (43). Instead of a traditional ‘diagnostic assessment’ approach of administering standardized tests that focus upon identifying an individual’s impairments, a ‘flip the rehab’ model starts with identifying the goals and expectations of the individual and family members, as well as the self-reported barriers to achieving their goals. This process is then followed by assessments to help document strengths and weaknesses to assist with achieving the therapy goals.

**Current barriers to provision of SLT services across the UK, USA and Australia**

So why are all individuals with PPA not being seen by SLT services? It is clear that there are number of barriers that may limit access.

**Firstly, many individuals with PPA are never referred to SLT in the first place.** This may be associated with a scepticism on the part of the referrer, due to the lack of evidence that these interventions are clinically meaningful for the person with PPA. Yet, there is undoubtedly a lack of awareness of the breadth of the SLT role and the potential benefit of non-pharmacological interventions for PPA across the healthcare community. Neurologists refer to SLT more often than other professionals, across the UK and Australia (30,44), perhaps due to their familiarity with the SLT role with people with post-stroke aphasia.

Secondly, the availability of SLT services specifically for people with PPA is limited – many individuals are seen by SLT services without any experience of PPA and therefore may have an
inadequate assessment or management plan – specialist services are currently sparsely and inequitably distributed e.g. a review of SLTs in the UK National Health Service found little available resources in some areas and much more in others, with wide geographical variation (30). While most SLTs receive training in graduate school on how to evaluate and provide treatment for individuals with stroke-induced aphasia, many students do not receive formal training in the area of PPA. This leads to a lack of confidence amongst SLTs in their ability to work with this patient group (44). SLTs without the proper training may be unaware of how to adapt evidence-based interventions for a neurodegenerative condition or how to write reimbursable goals for individuals with a progressive aphasia. Consequently, individuals may be discharged prematurely, rather than providing the ongoing treatment and support that is needed for this condition.

Thirdly, SLT research in PPA has been limited and so many interventions rely on expert evidence rather than studies demonstrating clear effectiveness – this has resulted in the lack of professional guidelines for SLT interventions in PPA. In the UK, the Royal College of Speech and Language Therapy position paper has outlined the role of a SLT in the differential diagnosis of FTD and PPA, in training family carers and health and social care staff, and refers the reader to the research literature on interventions. Unfortunately, the research literature that underpins this position paper is limited and whilst approaches described under person-centred dementia care are assumed to inform care across the dementias, commonly used therapies within such approaches including reminiscence and life story work have largely been developed for those with memory rather than language difficulties (45).
Finally, there is the more complex issue of commissioning of services (e.g. in the UK) and insurance reimbursement (e.g. in the US), the latter often resulting in a financial burden for people with PPA and their families. In the UK National Health Service, on average SLTs are able to offer only four therapy sessions to people with PPA, with many services being limited to single assessment and advice sessions. In the US, because the onset of PPA often occurs under the age of 65, many diagnosed individuals do not have access to their Medicare benefits for therapy services. Private insurances, such as Blue Cross Blue Shield, United Health Care, Aetna, or Cigna, all have different policies in terms of their coverage of therapy for neurodegenerative conditions, with some plans stating that they do not cover “rehabilitation services” for progressive conditions where symptoms will worsen over time. More positively, Medicare in the US has recently instated an important coverage change, which is relevant for individuals with PPA, whereby “coverage for therapy and nursing services is based on a beneficiary’s need for skilled care, not on the ability to improve”. It is also expected that the recent implementation of the Australian National Disability Insurance Scheme (NDIS) will break down barriers to services for those with younger onset dementia syndromes.

**Future priorities**

At present SLTs face the task of maximising the efficient use of limited resources in clinical practice. Restrictive referral criteria and priority schedules mean that providing best care is not always straightforward. Future priorities in this area should target: 1) education for all healthcare providers on the potential benefit of SLT for people with PPA; 2) education and training for SLTs
across graduate school programs regarding PPA; 3) development of a set of evidence-based speech and language therapy clinical practice guidelines for assessment and management of; and 4) advocacy efforts to increase available services and insurance reimbursement for SLT for PPA, in addition to coverage of telemedicine services for this population to increase access to care.

Nearly all individuals with PPA have the potential to benefit from person-centred SLT (see Table 3). Identifying the variables that impact the potential benefits of treatment will be important, and may include things such as the presence of an engaged care partner in treatment sessions, motivation, and anosognosia for their deficits. Furthermore, attempting to identify the ideal candidates for different approaches at each stage of disease progression will be useful. Some interventions are often difficult to test with conventional trial methods, meaning an n-of-1 trial methodology may be preferable in some situations. Nevertheless, research, particularly longitudinal studies with larger groups, will provide information about if, and how, a broad range of speech and language approaches can better meet the needs of people with PPA and their families. Table 4 provides an overview of the type of studies currently available.

SLTs also require accessible evidence-based resources in this area. Developing internet-based resources such as the Better Conversations with PPA package (34) will deliver free therapy resources. Similarly the Communication Bridge telemedicine clinical trial (36), currently underway, will provide information about the effectiveness of delivering therapy remotely. There is work underway exploring what individuals with PPA themselves would like SLTs to research and provide clinically, and how overall quality of life for people with PPA may be improved (46).
Little is known about what people with PPA and their families feel is a priority for their conversations and relationships or their support from services more generally.

**Conclusion**

People with PPA should routinely be referred for SLT interventions. Care pathways that direct physicians to refer to speech and language therapy services will provide equity of access and care. Health care funders need to reconsider how they reimburse non-pharmacological interventions, such as speech and language therapy, that can potentially maintain people’s independence for longer. SLTs can provide a broad variety of interventions to meet the needs of people with PPA and their families. As a profession SLTs are becoming more skilled in delivering these interventions and the research literature in this area is rapidly developing. More evidence in this area will continue to reduce many of the barriers, enabling more people with PPA and their families to access evidence-based speech and language therapy.
Acknowledgments

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Figure 1 – A clinical ‘roadmap’ for diagnosing the primary progressive aphasia (PPA) subtypes – adapted from Marshall et al, 2018 (see for more details). svPPA = semantic variant, nfvPPA = nonfluent variant, lvPPA = logopenic variant. ‘Atypical’ PPA here includes the unclassified or not otherwise specified group of patients.
Figure 2 – Classical neuroimaging features of the PPA variants – svPPA = semantic variant, nfVPPA = nonfluent variant, lvPPA = logopenic variant, NOS = not otherwise specified. Longitudinal imaging patterns at baseline and approximately one year and two years from baseline – top row shows coronal sections and bottom row shows axial sections (left hemisphere on right of picture for both): A) asymmetrical anteroinferior temporal lobe atrophy in svPPA; B) asymmetrical postero-inferior frontal and insular atrophy in nfVPPA; C) asymmetrical posterior-superior temporal and inferior parietal atrophy in lvPPA; D) widespread left hemispheric atrophy in PPA-NOS (in this case due to a progranulin mutation).
Figure 3 – Clinico-pathological correlations in primary progressive aphasia (adapted from Bergeron et al, 2018). Aβ is Alzheimer’s pathology; PiD is Pick’s disease, CBD is corticobasal degeneration, PSP is progressive supranuclear palsy (all forms of tauopathy); TDP-A, TDP-B, TDP-C and TDP-U (unclassified) are all forms of TDP-43 proteinopathy. svPPA = semantic variant primary progressive aphasia, nfvPPA = nonfluent variant, lvPPA = logopenic variant, PPA-M/U here represents a mixed-unclassified variant, equivalent to the PPA-NOS group discussed in the text.
Figure 4 – Examples of interventions used for people with primary progressive aphasia

<table>
<thead>
<tr>
<th>Word retrieval interventions</th>
<th>Script training</th>
<th>Compensatory strategies</th>
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<tbody>
<tr>
<td>Using Repetition and Reading in the Presence of a Picture in a word retrieval intervention (13)</td>
<td>Hierarchy of intervention tasks used to promote use of scripts in conversations (19)</td>
<td>Using an AAC device - SemAssist software on a computer to enable a person with primary progressive aphasia to complete cooking tasks (25)</td>
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</table>

**Word retrieval interventions**

**Examples**

- Using Repetition and Reading in the Presence of a Picture in a word retrieval intervention (13)

**Script training**

**Example 1** (easy):

**Script:**

"Football is a great sport. My favorite NFL team is the Green Bay Packers. My college team is the UW Badgers. I love watching football all the time."

**Example 2** (hard):

**Script:**

"Fly-fishing is a passion of mine for numerous reasons, but mostly for the wonderful places it takes me to. The waters and the ecosystems are inevitably beautiful and interesting. I also enjoy the fact that fly-fishing is so demanding, challenging and totally absorbing. It serves a therapeutic role that releases me from the stresses of everyday life. When I am not fishing, I often find myself planning a trip to one of the places I love to fish most, including Connecticut, Montana, Alaska, Canada, or Texas."
Table 1: Clinical and neuropsychological features of the primary progressive aphasia variants
(adapted from Woollacott et al, 2016) – svPPA = semantic variant, nfvPPA = nonfluent variant, lvPPA = logopenic variant.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>svPPA</th>
<th>nfvPPA</th>
<th>lvPPA</th>
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<tbody>
<tr>
<td>Spontaneous speech (fluency, errors, grammar, prosody)</td>
<td>Fluent, garulous and circumlocutory, semantic errors, intact grammar and prosody</td>
<td>Slow and hesitant, effortful ± apraxic, phonetic errors, may be agrammatic, a prosodич</td>
<td>Hesitant, not effortful or apraxic, frequent word-finding pauses and loss of train of sentence, intact grammar, intact prosody</td>
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<td>Naming</td>
<td>Severe anomia with semantic paraphasias</td>
<td>Moderate anomia with phonetic errors and phonemic paraphasias</td>
<td>Mild to moderate anomia with occasional phonemic paraphasias</td>
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<td>Single word comprehension</td>
<td>Poor</td>
<td>Intact early on, but affected later on</td>
<td>Intact early on, but affected later on</td>
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<td>Sentence comprehension</td>
<td>Initially preserved, later on becomes impaired as word comprehension is impaired</td>
<td>Impaired if grammatically complex</td>
<td>Impaired, especially if long</td>
</tr>
<tr>
<td>Single word repetition</td>
<td>Relatively intact</td>
<td>Mild to moderately impaired if polysyllabic, otherwise intact</td>
<td>Relatively intact (compared with sentence repetition)</td>
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<tr>
<td>Sentence repetition</td>
<td>Relatively intact</td>
<td>Can be effortful, impaired if grammatically complex</td>
<td>Impaired, with length effect</td>
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<tr>
<td>Reading</td>
<td>Surface dyslexia</td>
<td>Phonological dyslexia + phonetic errors on reading aloud</td>
<td>Phonological dyslexia</td>
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<tr>
<td>Writing</td>
<td>Surface dysgraphia</td>
<td>Phonological dysgraphia</td>
<td>Phonological dysgraphia</td>
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### Table 2: Regional and national support groups across the UK, the US and Australia.

<table>
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<th><strong>UK:</strong></th>
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<tr>
<td>Rare Dementia Support [which includes separate support groups for PPA (patients and carers), and all frontotemporal dementia (FTD) disorders (carers only)]</td>
<td><a href="http://www.raredementiasupport.org">www.raredementiasupport.org</a></td>
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<tr>
<td>Dyscover [a group for all forms of aphasia, but offers support for people with PPA and their partners]</td>
<td><a href="http://www.dyscover.org.uk">www.dyscover.org.uk</a></td>
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<td>Mesulam Centre for Cognitive Neurology and Alzheimer’s Disease</td>
<td><a href="http://www.brain.northwestern.edu/support/supportgroup/">www.brain.northwestern.edu/support/supportgroup/</a></td>
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Table 3: Key points in SLT interventions for primary progressive aphasia (PPA).

- Nearly all individuals with PPA have the potential to benefit from person-centred SLT.
- Interventions do not ‘cure’ speech and language difficulties but support people to be able to maintain independence for as long as possible.
- Participants should be referred to speech and language therapy as early as possible on their journey to allow person-centred interventions to be collaboratively planned and developed.
- Creative methods of service delivery are being explored and participants may benefit from being referred to national centres and research institutes to participate in new and evolving intervention studies.
Table 4: Overview of the design of speech and language therapy intervention studies in primary progressive aphasia

<table>
<thead>
<tr>
<th>Case study</th>
<th>Case series</th>
<th>Non-randomised, non-controlled trial</th>
<th>Non-randomised controlled trial</th>
<th>Randomised controlled trial</th>
<th>Systematic review</th>
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<td>Impairment based approaches - Word retrieval therapies</td>
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