EAJNS East African Journal of Neurological Sciences
Official journal of East African Association of Neurological Surgeons

Review Article EAJNS 4(3): 169-180

A Scoping Review of Neuropsychological and Neuroimaging Advances in Primary Progressive Apraxia of Speech (PPAOS)

Authors: Mohamed Taiebine[1], Saadia Aidi [2,3]

Affiliations

1. Euromed Research Centre, Euro-Mediterranean University of Fez (UEMF), Fez, Morocco
2. Department of Neurology and Neuropsychology, Speciality Hospital, Rabat, Morocco
3. Faculty of Medicine and Pharmacy, University of Mohammed V, Rabat, Morocco

Corresponding author: Mohamed Taiebine. Email: m.taiebine@ueuromed.org

Received: 07-03-2025; Revised 26-09-2025: Accepted: 26-09-2025
DOI: https://dx.doi.org/10.4314/eajns.v4i3.6

Abstract

Background: Primary progressive apraxia of speech (PPAOS) is a neurodegenerative disorder characterized by isolated speech production difficulties. Neuropsychological and neuroimaging investigations have contributed significantly to our understanding of this condition. This review aims to map recent advances in neuropsychological and neuroimaging research on PPAOS, highlighting their contributions to diagnosis, and clinical characterization. **Materials and methods**: This scoping review explored studies from four databases: MEDLINE, Web of Science, Google Scholar, and Scopus. A summary of clinical neuropsychological and neuroimaging characteristics has been depicted for the selected studies. **Results**: A total of twenty-four studies highlighted the necessity of assessing cognitive-linguistic and motor speech functions in PPAOS. Neuropsychological findings have refined the diagnostic criteria for PPAOS, differentiating it from other aphasic variants. Neuroimaging studies have identified progressive atrophy in brain regions crucial for speech motor planning and execution, providing valuable insights into the neural correlates of PPAOS. **Conclusion**: Advances in neuropsychology and neuroimaging have significantly enhanced our comprehension of PPAOS. These findings hold promise for improved diagnosis, differential diagnosis, and the development of targeted interventions. Future research should focus on longitudinal studies to elucidate disease progression and explore potential speech biomarkers for earlier screening clinically, cross-culturally and cross-linguistically

Keywords: Primary progressive apraxia of speech (PPAOS); neuropsychology; neuroimaging, speech production; neurodegeneration.

INTRODUCTION

This review examines the current understanding of progressive apraxia of speech (PAOS), particularly concentrating on its relatively unambiguous form—PAOS occurring without aphasia, now commonly termed primary progressive apraxia of speech (PPAOS). This distinction between primary progressive apraxia (PPA) and PAOS is crucial, as it affects clinical diagnosis, localization, prognosis, associated deficits, management strategies, and the underlying pathology of these disorders (1,2). In this context, PPAOS will

be defined as a clinical syndrome characterized predominantly by apraxia of speech (AOS), with minimal or ambiguous evidence of aphasia. The term AOS+PAA (progressive agrammatic/nonfluent aphasia) will denote the variant of PPA where AOS is most frequently observed, acknowledging that many studies interchangeably use the terms agrammatic and/or nonfluent PPA (nfPPA) for patients who may exhibit either or both conditions. The label nfPPA will be applied in instances of uncertainty regarding the presence of AOS. Conversely, when addressing patients with nfPPA where AOS is explicitly absent, the term PAA (progressive agrammatic aphasia) will be utilized (3).

Definition and clinical profiles of Primary Progressive Apraxia of Speech (PPAOS)

Primary progressive apraxia of speech (PPAOS) is characterized as a clinical syndrome in which apraxia of speech emerges as the primary and most significant symptom of a neurodegenerative disorder. This condition is marked by difficulties in planning or programming the motor patterns and actions required for speech production (1,4,5). It is important to differentiate PPAOS from primary progressive aphasia (PPA), where apraxia of speech may occur alongside other language impairments (1). PPAOS may manifest as an isolated condition or evolve to encompass additional neurological deficits over time (2).

The recognition of apraxia of speech within neurodegenerative syndromes dates back to the early 1990s, although it may have been acknowledged even earlier, albeit under different terminology (1). The limited number of cases documented in the past can be attributed, in part, to the challenges in distinguishing apraxia of speech from aphasia and dysarthria. For instance, Mesulam's case study presented not only aphasia but also "labored" and "dysarthric" speech, along with "buccofacial apraxia" (4). These symptoms could easily be linked to apraxia of speech, given the contemporary understanding of primary progressive aphasia and primary progressive apraxia of speech (4).

Recent research has uncovered potential subtypes of PPAOS, including phonetic and prosodic variants, each associated with unique neuroimaging findings and clinical features (5,6). Furthermore, PPAOS has been predominantly associated with specific neuropathologies, particularly tauopathies, rather than amyloid-related conditions (5). These insights highlight the diversity within PPAOS and its possible connections to other neurodegenerative disorders, such as corticobasal syndrome (7).

The differences in speech patterns observed in patients with PPAOS cannot be solely attributed to the severity of the condition or the effects of dysarthria or aphasia (8, 9). This observation suggests the existence of subtypes within PPAOS, a concept that has been considered for apraxia of speech for some time, regardless of the specific context.

Prevalence and epidemiology of PPAOS

PPAOS is identified as a rare neurodegenerative disorder, indicating its low prevalence in the general population. Current literature primarily emphasizes clinical features, subtypes, neuroimaging correlates, and the progression of PPAOS, rather than focusing on epidemiological data. The estimated global prevalence of Progressive Apraxia of Speech (PAOS) is approximately 4.4 per 100,000 when including patients with PPAOS and those with mild aphasia. The prevalence of PPAOS alone is likely around 2 per 100,000. The onset of symptoms typically occurs after the age of 65 for about two-thirds of affected individuals, although it can begin anywhere from the third to the ninth decade of life. Both genders are affected equally, and there is a noted tendency for non-right handedness among individuals with PPAOS (2,3).

While approximately 25% of patients report a family history of neurodegenerative diseases, only 5% have multiple first-degree relatives affected. The two most frequent underlying pathologies are Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD), which are both Parkinsonian disorders. As the disease progresses, PPAOS can also be associated with other motor impairments, cognitive deficits, and behavioral changes. Furthermore, PPAOS does not appear to be linked to an increased risk of genetic mutations that could be causative. Although PPAOS can persist as the primary deficit for extended periods, typically five years or more, it eventually progresses, leading to the emergence of additional neurological issues (1,10). Despite this progression, Apraxia of Speech (AOS) remains the most significant clinical deficit, with variability in the rate of progression and the timing of additional deficits among individuals (2).

Neuroimaging studies of PPAOS

Neuroimaging studies have revealed that neurodegeneration and brain atrophy in PPAOS are associated with specific regions of the brain (11, 12). Clinical and neuroimaging data indicate that abnormalities in the caudate nucleus, supplementary motor area (SMA), cingulate, insula, and Broca's area become evident over time, with motor cortex involvement and development of additional neurological symptoms occurring in later stages (13,14). Furthermore, voxel-based morphometry has demonstrated focal atrophy in the superior lateral premotor cortex and SMA, with white matter volume loss extending to the inferior premotor cortex and body of the corpus callosum (9). These findings are consistent with other studies that have observed grey matter atrophy and white matter tract degeneration in the frontal gyri, precentral cortex, and SMA (5).

Notably, there is evidence of distinct neuroimaging patterns associated with different subtypes of PPAOS, with the phonetic subtype exhibiting bilateral involvement of the SMA and cerebellar crus, and the prosodic subtype demonstrating more focal involvement (5). Moreover, longitudinal studies have demonstrated that rates of neurodegeneration in PPAOS correlate with functional connectivity to the premotor, motor, and frontal cortex, with connectivity to the caudate and thalamus more strongly associated with rates of hypometabolism than atrophy (12). This suggests that functional connectivity patterns may be indicative of the progression of neurodegeneration in PPAOS.

Based on the aforementioned clinical and epidemiological features of PPAOS, this current scoping review of the literature intends to inform readers on linguistic, cognitive, and neuroimaging perspectives in this neurodegenerative condition.

METHODS

Search Strategy: The articles were sourced from four databases: MEDLINE, Web of Science, Google Scholar, and Scopus. The search was conducted for articles published between 2010 and 2024, and the keywords used were (PPAOS OR primary progressive OR apraxia) AND speech AND (neuroimaging OR CT OR MRI OR DTI OR PET scan OR SPECT) AND (neuropsychological OR linguistic OR cognitive OR neurolinguistic).

Inclusion and Exclusion Criteria: This scoping review followed the guidelines of scoping review by Arksey & O'Malley (15) by including studies that met the following criteria: (a) the paper was published in English; (b) the article was a peer-reviewed, published paper that presented new data (excluding review and theoretical papers);

(d) the article included patients with PPAOS; and (e) the article focused on neuroimaging and/or neuropsychological findings in PPAOS.

Study Selection and extraction: A total of 574 articles were identified through database searches. 62 full-text studies were assessed for eligibility, and 24 articles were deemed eligible and included in this scoping review. To guarantee the reliability of the data, we established a comprehensive multi-tiered review procedure that involved cross-referencing data from various databases. Each article underwent a thorough assessment by the authors based on specific inclusion and exclusion criteria, and any inconsistencies were addressed through additional inquiry and validation by an independent referee. The data extraction process concentrated on collecting precise information in the following categories: reference, country, research design, aim of study, participants, linguistic and acoustic assessment, cognitive testing, neuroimaging features, languages addressed and outcomes.

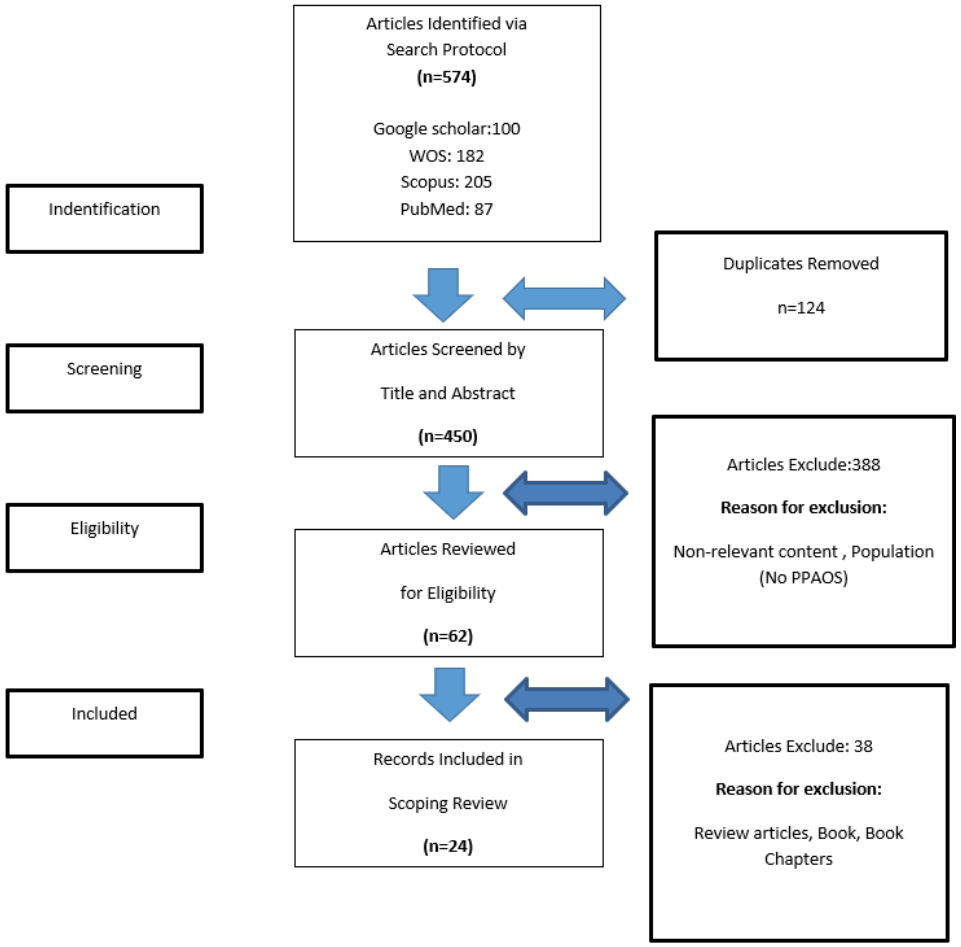

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews guidelines (PRISMA-ScR) flow diagram for the scoping review process (35).

RESULTS

A total of twenty-four studies examined PPAOS all stemming from the USA while one originated from Japan. In terms of research design, cross-sectional studies are the most common type of research design used in these studies (n=10), followed by prospective studies (n=4) and single case studies (n=4).

Regarding patients with PPAOS vs controls, the selected studies reveal a variety and significant disparity of patient-control ratios used in research on PPAOS. While some studies employ a 1:1 ratio, others utilize 1:2, 3:1, or even higher ratios. The choice of ratio often depends on factors such as the rarity of the condition, the availability of suitable controls, and the specific research questions being addressed.

Acoustic and linguistic assessment

In terms of acoustic and linguistic assessment, the testing tools reveal that the Western Aphasia Battery (WAB) and its revised version (WAB-R) are the most frequently used, appearing in 60% of the selected studies. The Apraxia of Speech Rating Scale (ASRS) and its version 3 (ASRS-3) are also commonly utilized, appearing in 50% of the studies on PPAOS. Other frequently employed assessments include the Boston Naming Test (BNT), the Token Test, and the Motor Speech Disorder (MSD) scale, each appearing in approximately 40% of the selected studies. The remaining assessment tools, such as the Northwestern Anagram Test (NAT), the Articulation Error Score (AES), and various speech tasks, are used less frequently, appearing in around 20-30%. This analysis highlights the prevalence of certain assessment tools in the evaluation of apraxia of speech, emphasizing their importance in clinical practice and research.

Neurocognitive testing

Regarding neuro-cognitive testing, the Montreal Cognitive Assessment (MoCA) emerges as the most frequently employed test, appearing in 60%. This suggests a strong preference for the MoCA as a comprehensive screening tool for cognitive function. Additionally, the Frontal Assessment Battery (FAB) is another commonly used test, featured in 50%. Other frequently used tests include the Mini-Mental State Examination (MMSE), Neuropsychiatric Inventory Questionnaire (NPI-Q), and the Trail Making Test (TMT). Additionally, the inclusion of tests such as the Unified Parkinson's Disease Rating Scale (UPDRS) highlights the importance of assessing specific cognitive domains, particularly in neurodegenerative conditions like Parkinson's disease.

Neuroimaging

The analysis of neuroimaging studies in PPAOS shows a diverse range of techniques employed. The most frequently used neuroimaging modalities are magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT). MRI, particularly with diffusion tensor imaging (DTI), is used to assess brain structure and white matter integrity. PET scans with tracers such as [18F]-fluorodeoxyglucose (FDG) and [18F]-AV-1451 are employed to evaluate brain metabolism and tau protein deposition. SPECT scans, while less common, have also been used to investigate brain blood flow and metabolism. In terms of frequency, MRI and PET scans are the most prevalent neuroimaging techniques utilized in PPAOS research, with DTI and FDG-PET being particularly common.

Neuroimaging techniques provide critical insights into the neuropathology of PPAOS and related aphasias, forming a neuroanatomical basis for their clinical classification. Studies using PET, MRI, and DTI have consistently revealed distinct patterns of brain atrophy and hypometabolism. For example, Josephs et al. (20) utilized [18F]-fluorodeoxyglucose (FDG)-PET to identify prerolandic hypometabolism in patients with nonfluent speech, including PPAOS, a pattern not seen in fluent aphasia. This finding helps differentiate clinical presentations. Furthermore, Josephs et al. (4) expanded on this by showing that PPAOS is associated with atrophy in the superior

lateral premotor cortex and supplementary motor area (SMA), as well as a reduction in white matter volume extending to the inferior premotor cortex and corpus callosum. The distinctive nature of PPAOS was further supported by DTI findings of decreased fractional anisotropy in the superior longitudinal fasciculus (4), distinguishing it from other primary progressive aphasias. A case study by Uyama et al. (31) reinforced this, showing that apraxia of speech (AOS)-related brain lesions are frequently located in the left hemisphere, particularly the precentral gyrus and pars opercularis, which are crucial for speech motor function.

Expanding on regional brain changes, a comparison between PPAOS and progressive supranuclear palsy (PSP) by Whitwell et al. (11) showed that while PPAOS is characterized by localized grey matter loss in the superior premotor cortex, PSP involves more widespread atrophy. Despite this difference, both syndromes showed midbrain atrophy, suggesting a degree of shared pathophysiology. Similarly, Josephs et al. (1) found that PPAOS is associated with extensive atrophy and hypometabolism across multiple regions, including the premotor cortex, prefrontal cortex, motor cortex, and basal ganglia, with some patients progressing to syndromes resembling PSP.

In addition to structural changes, functional connectivity and metabolic patterns provide further clues. Botha et al. (18) discovered that PPAOS patients have reduced connectivity between the right SMA and left posterior temporal gyrus. This reduced connectivity correlated with the severity of articulatory deficits, emphasizing the SMA's crucial role in PPAOS pathophysiology. In a separate study, Botha et al. (19) documented bilateral hypometabolism in PPAOS patients and noted a higher prevalence of non-right-handedness in this population, suggesting a possible susceptibility factor.

Recent research has also explored tau pathology as a biomarker for PPAOS. Utianski et al. (5) demonstrated that PPAOS patients have increased tau accumulation in the precentral gyrus, SMA, and Broca's area—with tau in Broca's area specifically correlating with aphasia. Further work by Utianski et al. (21) showed that patients with aphasic PPA and AOS have a broader distribution of tau accumulation compared to those without AOS. This aligns with findings from Tetzloff et al. (23), who documented the progression of abnormalities in a corticobasal degeneration patient from speech-related areas to the motor cortex. Other studies, such as Seckin et al. (14), utilized FDG-PET to identify asymmetric hypometabolism, proposing PPAOS may be an early sign of Parkinson's plus disorder. Moreover, Utianski et al. (26) confirmed that flortaucipir PET is effective for monitoring progression in these tauopathies. Finally, Josephs et al. (9) linked slower diadochokinetic (DDK) rates to hypometabolism in the right cerebellar dentate and left SMA, directly connecting apraxia severity to specific metabolic changes. Robinson et al. (28) highlighted the clinical relevance of hemispheric lateralization by finding that PPAOS patients with a right-dominant pattern of hypometabolism experienced the most rapid behavioral and motor decline.

DISCUSSION

This scoping review on PPAOS reveals several key findings. Firstly, the majority of studies originate from the USA, highlighting a potential research bias. Secondly, cross-sectional studies predominate, while prospective studies are less common. Thirdly, there is a significant disparity in patient-control ratios across studies,

reflecting the challenges of recruiting and studying this rare condition. Neuroimaging techniques, particularly MRI and PET, play a crucial role in investigating brain structure and function in PPAOS. DTI and FDG-PET have provided valuable insights into the neurodegenerative processes underlying the condition. They consistently point towards abnormalities in brain regions critical for speech production, such as the premotor cortex, supplementary motor area, and Broca's area.

In terms of neuropsychological findings, they indicate that PPAOS is associated with various cognitive impairments, including slowed speech, impaired motor planning, and cognitive deficits. Regarding assessment tools, the Western Aphasia Battery (WAB) and the Apraxia of Speech Rating Scale (ASRS) are the most frequently employed, highlighting their clinical significance.
Overall, the selected studies indicate that PPAOS is characterized by a range of neuropsychological and neuroimaging abnormalities. Patients with PPAOS exhibit slower diadochokinetic (DDK) rates, correlated with the severity of apraxia. Neuroimaging studies reveal increased tau deposition in specific brain regions, particularly Broca's area, associated with aphasia. Cognitive impairments, such as deficits in response inhibition, are also observed in some patients. Functional connectivity studies highlight the role of the SMA in the pathophysiology of PPAOS. The underlying neuropathology of PPAOS is diverse, with evidence for tauopathies, TDP-43 inclusions, and neurodegenerative processes. These findings contribute to a better understanding of the clinical features, neuroanatomical correlates, and progression of PPAOS.

Neuropsychology of PPAOS: Behavioral symptoms and cognitive deficits

PPAOS is characterized by a gradual loss of speech production abilities, with behavioral symptoms and cognitive deficits that can vary depending on the individual case (3, 16). The neuropsychological profile of a patient with PPAOS may include primary deficits in expressive language, such as difficulties with oral and written production, verbal fluency, and repetition, as well as milder executive functioning deficits (4, 9, 17-19). Additionally, patients may exhibit trial-and-error articulatory attempts, groping, and distorted substitutions, which are indicative of PPAOS (1,9). Over time, patients with PPAOS may develop aphasia, dysarthria, cognitive and behavioral changes, and other neurological signs, suggesting a progression of the disease beyond speech production (2,5).

Interestingly, there is evidence of two distinct subtypes of PPAOS—Phonetic and Prosodic—each associated with different patterns of brain abnormalities and clinical manifestations (2,8). The phonetic subtype is characterized by distorted sound substitutions, while the prosodic subtype is marked by slow, segmented speech (2,6). These subtypes may have implications for the behavioral symptoms and cognitive deficits observed in patients with PPAOS.

Neuropsychology of PPAOS: medical comorbidities

PPAOS has been observed to evolve into or be associated with other neurological disorders over time. For instance, patients initially diagnosed with pure prosodic PPAOS were later found to develop corticobasal syndrome (CBS), as evidenced by the emergence of extrapyramidal symptoms (7,20). This suggests a potential connection between PPAOS and CBS, a neurodegenerative disorder characterized by movement and cognitive dysfunctions. Furthermore, PPAOS has been distinguished from primary progressive aphasia (PPA) but is recognized to co-occur

with progressive aphasia and other neurological deficits as the disease progresses (2). The relationship between PPAOS and movement disorders such as corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) is also of interest, as these conditions may share underlying pathophysiological mechanisms (1, 6, 21).

Interestingly, neuroimaging studies have revealed distinct patterns of brain abnormalities associated with PPAOS, which may relate to its connection with other neurological disorders. For example, hypometabolism and atrophy in specific brain regions such as the frontal gyri, precentral cortex, and SMA have been identified in PPAOS patients (21-23). These findings are consistent with the observed reduced connectivity of the right SMA in PPAOS participants, which may serve as a biomarker for the severity of the disorder (18, 19). Additionally, the pattern of hypometabolism in the lateral premotor cortex (LPC) and SMA has been linked to different clinical features and rates of progression in PPAOS, suggesting that the involvement of these regions may influence the connection to other neurological disorders.

Advances in neuroimaging and their clinical implications on understanding PPAOS

Recent advancements in neuroimaging have significantly enhanced our understanding of Primary Progressive Apraxia of Speech (PPAOS). Various neuroimaging techniques, including magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), fluorodeoxyglucose positron emission tomography (FDG-PET), and task-free functional magnetic resonance imaging (fMRI), have identified specific patterns of brain abnormalities associated with PPAOS (24). These methods have consistently revealed structural and metabolic alterations in the neural networks responsible for speech motor planning and execution. Notably, research has demonstrated hypometabolism, grey matter atrophy, and degeneration of white matter tracts in critical regions such as the frontal gyri, precentral cortex, and the supplementary motor area (SMA) (5,6,21).

Neuroimaging has been instrumental not only in diagnosing PPAOS but also in distinguishing its subtypes and providing prognostic insights. For instance, it has effectively differentiated between the phonetic and prosodic subtypes of PPAOS, each exhibiting unique imaging patterns indicative of distinct underlying pathologies (12,21). This differentiation is crucial for accurate diagnosis and for tailoring therapeutic interventions. Beyond subtyping, neuroimaging offers valuable prognostic information. Longitudinal studies have shown that PPAOS can precede corticobasal syndrome (CBS), a more extensive neurodegenerative disorder. These studies have identified specific neuroimaging markers, such as asymmetric cortical atrophy and decreased basal ganglia metabolism, that may predict this progression, thereby facilitating improved patient management (10).

These neuroimaging techniques have consistently demonstrated abnormalities in specific brain regions associated with speech production, including the premotor cortex, supplementary motor area (SMA), Broca's area, and the cerebellum. These regions are involved in motor planning, sequencing, and execution of speech movements. FDG-PET studies have revealed hypometabolism in areas such as the right cerebellar dentate, left SMA, and bilateral caudate nuclei. These findings suggest that impaired speech production in PPAOS is associated with reduced metabolic activity in brain regions critical for speech motor control. Tau-PET imaging has

shown increased tau protein deposition in regions like the precentral gyrus, supplementary motor area, and Broca's area, indicating the presence of neurodegenerative pathology in these areas. Structural MRI and VBM studies have identified atrophy in the premotor cortex, SMA, and other speech-related regions, suggesting neuronal loss in these areas. DTI has revealed abnormalities in white matter tracts connecting these regions, indicating disrupted communication between brain areas involved in speech production.

Moreover, functional neuroimaging has provided essential insights into the disrupted neural circuits in PPAOS. Task-free fMRI has demonstrated reduced functional connectivity within the speech and language network, particularly in the right SMA and the left posterior temporal gyrus (18,19). This finding is significant as it underscores the importance of these areas in the disorder's pathophysiology, suggesting that the clinical manifestations of PPAOS are not merely due to isolated structural damage but also result from a breakdown in communication between critical brain regions. The diminished connectivity in these areas highlights the complex nature of PPAOS as a network-level disorder rather than a focal lesion.

In summary, although PPAOS remains a challenging condition with a considerable impact on patients' quality of life, the integration of advanced neuroimaging techniques coupled with machine learning has led to significant progress in understanding its complex nature (32). Neuroimaging offers a powerful perspective on the structural and functional changes in the brains of individuals with PPAOS, providing insights into its etiology, classification, and potential future trajectory. Further research is essential to fully unravel the intricacies of this disorder. Collaborative efforts among neurologists, speech-language pathologists, neuropsychologists, and neuro-radiologists are crucial to advancing our understanding and improving clinical care (2,33, 34).

Limitations

This scoping review acknowledges several limitations that require thorough examination. Firstly, the geographical distribution of the studies reviewed is markedly uneven, with a predominant number originating from the United States. This geographic concentration restricts the applicability of the results to diverse populations and cultural settings. It is essential to recognize that the occurrence and clinical manifestations of PPAOS may differ significantly among various ethnic and cultural groups. Secondly, the dependence on a small selection of studies, especially those from Western nations, may have led to a publication bias. It is possible that studies yielding significant or statistically relevant outcomes were more frequently published, which could result in an inflated representation of certain findings while neglecting studies that report null or inconclusive results. Lastly, the diversity in research designs and methodologies among the studies included poses a considerable obstacle while exploring PPAOS in non-western populations. Differences in criteria for patient selection, assessment instruments, and data analysis methods complicate the ability to make meaningful comparisons and synthesize results across the various studies.

Clinical implications and future directions

The results of this scoping review carry significant clinical relevance for the diagnosis and treatment of PPAOS. Acknowledging the various neuropsychological and neuroimaging

characteristics associated with PPAOS underscores the necessity for a thorough assessment process that encompasses comprehensive assessments of speech and language, neuropsychological evaluations, and neuroimaging analyses. Furthermore, the detection of core neuropsychological deficits, including challenges in motor speech programming and executive functioning, can guide the development of specific and tailored interventions, such as speech-language therapy, cognitive rehabilitation, and effective communication strategies in cross-linguistic and multilingual clinical settings. Additionally, recognizing the possibility of extra-linguistic impairments and cognitive decline extending beyond mere speech and language issues underscores the critical need for continuous monitoring and follow-up of other neurodegenerative symptoms, including memory loss and changes in behavior.

Future investigations should aim to overcome the limitations identified in this scoping review. A key area of focus should be the examination of clinical, neuropathological, neuroimaging and neurobiological characteristics of PPAOS across various ethnic and cultural groups, as this is essential for comprehending the worldwide impact of the disorder despite its scarcity. Additionally, research should broaden its scope to include the long-term progression of PPAOS and its effects on individuals' quality of life. It is also important to assess the efficacy of different therapeutic approaches including pharmacological and non-pharmacological interventions. Furthermore, exploring the influence of genetic and environmental factors on the onset of PPAOS is a vital area of research. Finally, there is a need to create and validate assessment tools that are culturally sensitive, which involves modifying existing instruments and developing new measures that are appropriate for evaluating speech and language performances in diverse populations respecting the phonetic, phonological and phonotactic features of the targeted languages

CONCLUSIONS

This scoping review effectively captures the key findings of PPAOS, including clinical features, geographical bias, methodological heterogeneity, key neuroimaging findings, neuropsychological impairments, and the importance of standardized assessment tools. Recent investigations into PPAOS have significantly advanced our understanding of this neurodegenerative disorder. Neuropsychological assessments have been instrumental in delineating PPAOS from other aphasic variants, particularly agrammatic PPA. Neuroimaging studies have provided crucial insights into the neural correlates of PPAOS, demonstrating progressive atrophy in regions critical for speech motor planning and execution such as SMA. These findings have refined diagnostic criteria and contributed to earlier and more accurate identification of PPAOS. Therefore, there is an urgent need for cross-linguistic studies for patients speaking underrepresented languages in order to explore the intersection between speech, phonotactics and differential neurodegeneration in PPAOS.

Conflict of Interest

The authors declare no conflict of interest.

Funding

No sponsorship or funding arrangements relating to this article exist.

REFERENCES

1. Josephs KA, Whitwell JL. Progressive apraxia of speech and primary progressive aphasias. Movement Disorders in Dementias. 2014:213-30.
2. Duffy JR, Utianski RL, Josephs KA. Primary progressive apraxia of speech: From recognition to diagnosis and care. Aphasiology. 2021 Apr 3;35(4):560-91.
3. Botha H, Duffy JR, Whitwell JL, Strand EA, Machulda MM, Schwarz CG, Reid RI, Spychalla AJ, Senjem ML, Jones DT, Lowe V. Classification and clinicoradiologic features of primary progressive aphasia (PPA) and apraxia of speech. Cortex. 2015 Aug 1;69:220-36.
4. Josephs KA, Duffy JR, Strand EA, Machulda MM, Senjem ML, Master AV, Lowe VJ, Jack Jr CR, Whitwell JL. Characterizing a neurodegenerative syndrome: primary progressive apraxia of speech. Brain. 2012 May 1;135(5):1522-36.
5. Utianski RL, Duffy JR, Clark HM, Strand EA, Boland SM, Machulda MM, Whitwell JL, Josephs KA. Clinical progression in four cases of primary progressive apraxia of speech. American Journal of Speech-Language Pathology. 2018 Nov 21;27(4):1303-18.
6. Tetzloff KA, Duffy JR, Clark HM, Josephs KA, Whitwell JL, Utianski RL. Characterizing Speech Errors Across Primary Progressive Apraxia of Speech Subtypes. Journal of Speech, Language, and Hearing Research. 2024 Mar 11;67(3):811-20.
7. Kwon M, Shim WH, Jo Y, Park S, Lim JS, Lee JH. Pure prosodic type of primary progressive apraxia of speech mimicking nonfluent aphasia and later progressing to corticobasal syndrome. Alzheimer Disease & Associated Disorders. 2022 Oct 1;36(4):365-7.
8. Duffy, J. R., & Josephs, K. A. The diagnosis and understanding of apraxia of speech: Why including neurodegenerative etiologies may be important. Journal of Speech, Language, and Hearing Research. 2012 : 55(5), S1518–S1522.
9. Josephs KA, Duffy JR, Martin PR, Stephens YC, Singh NA, Clark HM, Botha H, Lowe VJ, Whitwell JL, Utianski RL. Acoustic analysis and neuroimaging correlates of diadochokinetic rates in mild-moderate primary progressive apraxia of speech. Brain and language. 2023 May 1;240:105254.
10. Garcia-Guaqueta DP, Botha H, Utianski RL, Duffy JR, Clark HM, Goodrich AW, Pham NT, Machulda MM, Baker M, Rademakers R, Whitwell JL. Progression to corticobasal syndrome: a longitudinal study of patients with nonfluent primary progressive aphasia and primary progressive apraxia of speech. Journal of Neurology. 2024 Apr 7:1-2.
11. Whitwell JL, Duffy JR, Strand EA, Xia R, Mandrekar J, Machulda MM, Senjem ML, Lowe VJ, Jack Jr CR, Josephs KA. Distinct regional anatomic and functional correlates of neurodegenerative apraxia of speech and aphasia: an MRI and FDG-PET study. Brain and language. 2013 Jun 1;125(3):245-52. 5
12. Sintini I, Duffy JR, Clark HM, Utianski RL, Botha H, Machulda MM, Senjem ML, Strand EA, Schwarz CG, Lowe VJ, Jack CR. Functional connectivity to the premotor cortex maps onto longitudinal brain neurodegeneration in progressive apraxia of speech. Neurobiology of aging. 2022 Dec 1;120:105-16.
13. Tetzloff KA, Duffy JR, Strand EA, Machulda MM, Boland SM, Utianski RL, Botha H, Senjem ML, Schwarz CG, Josephs KA, Whitwell JL. Clinical and imaging progression over 10 years in a patient with primary progressive apraxia of speech and autopsy-confirmed corticobasal degeneration. Neurocase. 2018 Mar 4;24(2):111-20.
14. Seckin ZI, Whitwell JL, Utianski RL, Botha H, Ali F, Duffy JR, Clark HM, Machulda MM, Jordan LG, Min HK, Lowe VJ. Ioflupane 123I (DAT scan) SPECT identifies dopamine receptor dysfunction early in the disease course in progressive apraxia of speech. Journal of neurology. 2020 Sep;267:2603-11.
15. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International journal of social research methodology. 2005 Feb 1;8(1):19-32. https://doi.org/10.1080/1364557032000119616
16. Botha H, Duffy JR, Strand EA, Machulda MM, Whitwell JL, Josephs KA. Nonverbal oral apraxia in primary progressive aphasia and apraxia of speech. Neurology. 2014 May 13;82(19):1729-35.
17. Josephs KA, Duffy JR, Fossett TR, Strand EA, Claassen DO, Whitwell JL, Peller PJ. Fluorodeoxyglucose F18 positron emission tomography in progressive apraxia of speech and primary progressive aphasia variants. Archives of neurology. 2010 May 1;67(5):596-605.
18. Botha H, Duffy JR, Whitwell JL, Strand EA, Machulda MM, Spychalla AJ, Tosakulwong N, Senjem ML, Knopman DS, Petersen RC, Jack Jr CR. Non-right handed primary progressive apraxia of speech. Journal of the neurological sciences. 2018 Jul 15;390:246-54.
19. Botha H, Utianski RL, Whitwell JL, Duffy JR, Clark HM, Strand EA, Machulda MM, Tosakulwong N, Knopman DS, Petersen RC, Jack Jr CR. Disrupted functional connectivity in primary progressive apraxia of speech. NeuroImage: Clinical. 2018 Jan 1;18:617-29.
20. Josephs KA, Duffy JR, Strand EA, Machulda MM, Senjem ML, Gunter JL, Schwarz CG, Reid RI, Spychalla AJ, Lowe VJ, Jack Jr CR. The evolution of primary progressive apraxia of speech. Brain. 2014 Oct 1;137(10):2783-95.
21. Utianski, R. L., Whitwell, J. L., Schwarz, C. G., Duffy, J. R., Botha, H., Clark, H. M., Machulda, M. M., Senjem, M. L., Knopman, D. S., Petersen, R. C., Jack, C. R., Jr, Lowe, V. J., & Josephs, K. A. Tau uptake in agrammatic primary progressive aphasia with and without apraxia of speech. European journal of neurology. 2018 *25*(11), 1352–1357.
22. Utianski RL, Duffy JR, Clark HM, Strand EA, Botha H, Schwarz CG, Machulda MM, Senjem ML, Spychalla AJ, Jack Jr CR, Petersen RC. Prosodic and phonetic subtypes of primary progressive apraxia of speech. Brain and language. 2018 Sep 1;184:54-65.

23. Tetzloff KA, Utianski RL, Duffy JR, Clark HM, Strand EA, Josephs KA, Whitwell JL. Quantitative analysis of agrammatism in agrammatic primary progressive aphasia and dominant apraxia of speech. Journal of Speech, Language, and Hearing Research. 2018 Sep 19;61(9):2337-46.
24. Spengler D, Baerga DR, Pattany P, Gomes-Osman J, Adams D, Luca C. Localization of primary progressive apraxia of speech using functional MRI–a case study (P4. 196). Neurology. 2017 Apr 18;88(16_supplement):P4-196.
25. Utianski RL, Martin PR, Hanley H, Duffy JR, Botha H, Clark HM, Whitwell JL, Josephs KA. A longitudinal evaluation of speech rate in primary progressive apraxia of speech. Journal of Speech, Language, and Hearing Research. 2021 Feb 17;64(2):392-404.
26. Utianski RL, Martin PR, Botha H, Schwarz CG, Duffy JR, Petersen RC, Knopman DS, Clark HM, Butts AM, Machulda MM, Jack Jr CR. Longitudinal flortaucipir ([18F] AV-1451) PET imaging in primary progressive apraxia of speech. Cortex. 2020 Mar 1;124:33-43.
27. Ash S, Nevler N, Irwin DJ, Shellikeri S, Rascovsky K, Shaw L, Lee EB, Trojanowski JQ, Grossman M. Apraxia of Speech in the Spontaneous Speech of Nonfluent/Agrammatic Primary Progressive Aphasia. Journal of Alzheimer's Disease Reports. 2023 Jan 1;7(1):589-604.
28. Robinson CG, Duffy JR, Clark HA, Utianski RL, Machulda MM, Botha H, Singh NA, Pham NT, Ertekin-Taner N, Dickson DW, Lowe VJ. Clinicopathological associations of hemispheric dominance in primary progressive apraxia of speech. European journal of neurology. 2023 May;30(5):1209-19.
29. Meade G, Pham NT, Schwarz CG, Clark HM, Duffy JR, Senjem ML, Lowe V, Botha H, Whitwell JL, Josephs KA, Utianski RL. The yes–no reversal phenomenon in patients with primary progressive apraxia of speech. Cortex. 2024 Aug 1;177:28-36.
30. Meade G, Whitwell JL, Dickson DW, Duffy JR, Clark HM, Ahlskog JE, Machulda MM, Josephs KA, Utianski RL. Primary Progressive Apraxia of Speech Caused by TDP-43: A Case Report. Neurology: Genetics. 2024 Mar 19;10(2):e200134.
31. Uyama N, Yokochi F, Bandoh M, Mizutani T. Primary progressive apraxia of speech (AOS) in a patient with Pick's disease with Pick bodies: a neuropsychological and anatomical study and review of literature. Neurocase. 2013 Feb 1;19(1):14-21.
32. Dial H, Pugalenthi LS, Gnanateja GN, Li JJ, Henry ML. Application of machine learning and temporal response function modeling of EEG data for differential diagnosis in primary progressive aphasia. Scientific Reports. 2025 Aug 12;15(1):29539.
33. Taiebine M, Keegan LC. Telepractice for bilingual and multilingual people with aphasia: a scoping review. Aphasiology. 2024 Jul 4:1-23.
34. Taiebine M, Aidi S, Benabdeljlil M, Faris ME. Neurolinguistic analysis of a case of crossed apraxia of speech in Arabic. International Journal of Brain and Cognitive Sciences. 2017;6(2):21-5.
35. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MD, Horsley T, Weeks L, Hempel S. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Annals of internal medicine. 2018 Oct 2;169(7):467-73.