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The Diagnosis and Understanding of Apraxia of Speech: Why Including Neurodegenerative Etiologies May Be Important

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Abstract

Purpose—To discuss apraxia of speech (AOS) as it occurs in neurodegenerative disease (progressive AOS, or PAOS) and how its careful study may contribute to general concepts of AOS and help refine its diagnostic criteria.

Method—The paper summarizes our current understanding of the clinical features and neuroanatomical and pathologic correlates of PAOS and its relationship to primary progressive aphasia (PPA). It addresses similarities and differences between PAOS and stroke-induced AOS that may be relevant to improving our understanding of AOS in general.

Conclusions—PAOS is clinical disorder that should be distinguished from PPA. Its recognition is important to clinical care provided by speech-language pathologists, but it also has implications for neurologic localization and diagnosis, and prediction of underlying pathology and histochemistry. The clinical features of PAOS and stroke-induced AOS have not been explicitly compared, but they may not be identical because PAOS does not follow a vascular distribution, the brunt of cortical pathology is in the premotor and supplementary motor area, and its onset, rather than acute, is slowly progressive with potential for adaptation to gradual impairment. Careful description and study of PAOS may be a valuable source of information for refining our understanding of AOS in general.

Keywords

apraxia of speech; progressive apraxia of speech; primary progressive aphasia; motor speech programming

Although the most current and widely accepted defining clinical features of apraxia of speech (AOS) (McNeil, Robin, & Schmidt, 2009; Wambaugh, Duffy, McNeil, Robin, & Rogers, 2006) are not tied to any specific etiology, stroke is the most frequent cause of AOS (Duffy, 2005; Ogar, Slama, Dronkers, Amici, & Gorno-Tempini, 2005) and the most frequent etiology reported in the vast majority of historic and recently published studies from which its diagnostic criteria have evolved. Among non-degenerative etiologies, stroke is also more likely to induce AOS in a predominant or “pure” form, without the “contaminating” cognitive deficits or other motor speech disorders induced by diffuse or multifocal conditions such as infection or trauma.

In recent years, it has been recognized that AOS can be caused by neurodegenerative conditions that emerge insidiously and progress slowly. In some cases, AOS is the only or the most prominent sign of neurodegenerative disease, or the predominant communication disorder when it coexists with primary progressive aphasia (PPA) or dysarthria (Duffy, 2006; Josephs et al., 2006; Josephs et al., in press; Ogar, Dronkers, Brambait, Miller & Gorno-Tempini, 2007). When AOS is the only or the clearly predominant neurologic problem, it is appropriately referred to as *primary* progressive apraxia of speech, or PPAOS (Duffy and McNeil, 2008). As such, neurodegenerative or progressive AOS (PAOS) may be a rich source of data for supporting or refining diagnostic criteria for AOS, and for improving our understanding of its underlying mechanisms. Attention to PAOS is also warranted because its management differs from that for AOS due to stroke or other non-degenerative causes.

The primary purposes of this paper are to (1) briefly discuss the association of AOS with neurodegenerative disease, (2) identify obvious and possible differences between stroke-induced AOS and PAOS, and (3) identify reasons for including neurodegenerative etiologies in studies of AOS. The paper is not intended to represent a comprehensive or critical review of the literature on AOS or PAOS. We have largely limited our review and citations to examples of work that help support the primary opinion expressed here that the study of PAOS can contribute to refinement of diagnostic criteria for AOS and our understanding of the disorder's underpinnings.

NEURODEGENERATIVE DISEASE AND AOS

The modern concept of what is now known as primary progressive aphasia (PPA) was introduced three decades ago in Mesulam's seminal paper on "slowly progressive aphasia" (Mesulam, 1982). Today, PPA is a well-established clinical entity and is the most widely recognized and studied "focal" neurodegenerative cognitive disorder (Duffy, 2006). Different PPA subtypes, with neuroimaging correlates, have now been recognized and operationally defined (Gorno-Tempini et al., 2011).

In contrast, until recently the association of AOS with neurodegenerative disease has been largely ignored or under-recognized (Duffy & McNeil, 2008). In the 1990s, case reports began to document AOS as the first or predominant sign of neurodegenerative disease. Clinical descriptions were often poor, however, and terms other than AOS were frequently used to label it (e.g., nonfluent progressive aphasia, slowly progressive anarthria, progressive aphemia, phonologic disintegration), but at least some of the speech features, when described, roughly corresponded to those associated with AOS. Numerous subsequent studies have more clearly defined both the disorder and the clinical milieu in which it occurs (e.g., Duffy, 2006; Joseph et al., 2006, in press; Ogar et al., 2007). Nonetheless, PAOS often remains hidden from full view because many studies bury it under PPA classifications, particularly within the nonfluent or agrammatic variant (Gorno-Tempini et al., 2011).

As a sign of neurodegenerative disease, PAOS may be uncommon, but it is probably not extremely rare. Several studies have documented that AOS is commonly present in progressive nonfluent/agrammatic aphasia (PNFA). For example, Ogar et al. (2007) documented PAOS in all of 18 consecutive patients with PNFA. Kertesz, Davidson, McCabe, Takagi, & Munoz (2003) reported that 9% of 67 patients with a diagnosis of PPA actually had a predominantly "aphemic" speech deficit. Duffy (2006) summarized 80 cases in which AOS was the first symptom in 80% of cases; among the 80 cases, 11% had no aphasia or dysarthria, and AOS was never less severe than any aphasia when aphasia was present. And, recent studies have confirmed that PPAOS can occur in the absence of aphasia (e.g., Josephs et al., 2006; Josephs et al., 2010).¹

It is reasonable to conclude from this brief review that PAOS (including PPAOS) can be considered an established clinical entity.

ARE THE CLINICAL MANIFESTATIONS OF STROKE-INDUCED AOS AND PAOS IDENTICAL?

Clinical features

There are no studies that directly compare the clinical manifestations of stroke-induced AOS to PAOS.² In fact, few studies have provided detailed description of the speech features that have led to a diagnosis of PAOS. This shortcoming is a source of legitimate criticism of many of the reports that make up the evidence supporting the existence of the disorder. Nonetheless, some studies have described speech characteristics sufficiently to support the diagnosis of PAOS using currently accepted core diagnostic criteria. For example, Duffy's (2006) retrospective study of 80 patients with PAOS documented in all subjects at least several AOS features (e.g., slow rate, distorted substitutions and additions, syllable segmentation, increased errors with increasing utterance length, articulatory groping and false starts/restarts). Josephs et al. (2006) noted similar characteristics among each of their 11 prospectively studied patients with PAOS.

The available data suggest that stroke-induced AOS and PAOS share many deviant speech features. Without formal comparisons, however, it would be premature to conclude that the patterns of speech abnormalities associated with AOS due to stroke versus neurodegenerative disease are indistinguishable. Some limited data do hint at differences. For example, Duffy (2006) noted the presence of reduced words per breath group during conversational or narrative speech despite grossly normal maximum vowel prolongation in 26% of 70 PAOS patients for whom the feature was noted, and for whom accompanying dysarthria was not felt to be a sufficient alternative explanation for the feature. This feature has not been described in studies of stroke-induced AOS. It is reasonable to hypothesize that it reflects a problem with speech planning because length of utterance per breath group is correlated with the depth of the inspiration that precedes it (Whitworth, Davis, Adams, & Ellis, 1995), implying that depth of inspiration preceding speech must be planned. Thus, consistently reduced syllables per breath group in some people with PAOS may reflect limitations on the amount of pre-utterance speech planning that can be accomplished. Speculatively, this might reflect a primary problem with speech breathing planning or it might be an artifact, for example, of limits on the number of syllables (rather than breath group length) that can be planned in advance of speech initiation. If this characteristic, regardless of its underlying nature, is unique to PAOS, it may have considerable diagnostic importance relative to establishing etiology; it may also provide an opportunity to improve our understanding of speech breathing planning. Similarly, stroke-induced AOS may have features that are not evident in PAOS, which would be of comparable etiologic diagnostic value.

¹Spastic and/or hypokinetic dysarthria are not uncommon when PAOS is more severe than or occurs without aphasia (Josephs et al., 2006; Josephs et al., in press; Ogar et al., 2007).

²Patterson, Graham, Lambon Ralph, and Hodges (2006) and Thompson, Ballard, Tait, Weintraub, and Mesulam (1997) have compared spoken language performance in patients with nonfluent or agrammatic Broca's aphasia due to stroke to patients with neurodegenerative nonfluent aphasia and found both similarities and differences. Although the patients studied may have had AOS, the designation of AOS was not used and speech was insufficiently described to be certain if AOS was present in some or all patients. Both studies concluded that a fuller understanding of PNFA would benefit from attention to its similarities and differences from stroke-induced non-fluent or agrammatic Broca's aphasia.

Clinical course

The differences are obvious. Stroke-induced AOS, in which there has been direct and radical destruction of neurons that serve the speech programming network, is typically most severe at onset, usually improves, and then becomes chronic if full recovery does not occur. PAOS begins insidiously and progresses slowly. Its evolution reflects the gradual “loss” of speech programming integrity, but very possibly within a context of some capacity to adapt to the slowly progressing deficits.

The gradual deterioration of speech in PAOS may reflect a variant of the serial lesion effect in which slow growing CNS lesions, or a series of successive contiguous lesions, may produce only mild deficits despite extensive involvement of critical brain structures (Ramirez, 1997; Rosen, Stein, & Butters, 1971). Thus, even when lesion loci and volume are comparable, the gradual, cumulative lesion burden from small serial lesions, or slow growing space occupying lesions, or, perhaps in the case of PAOS, the slow accumulation of synaptic loss, gliosis, and protein deposition in a single or multiple areas of the brain, results in less performance loss compared to that of a single acute lesion. In addition, the behavioral impairments may be *different in character* between acute and slowly accumulated damage, as suggested in the preceding section. For example, the cognitive, language, and behavioral consequences of tumors versus stroke in similar brain locations can be radically different (Anderson, Damasio, & Tranel, 1990).

Anatomic and pathologic correlates

There is emerging evidence that PAOS may predict localization and underlying pathology and histochemistry, and that its localization may not be identical to that often associated with stroke-induced AOS. When PAOS is isolated or predominant (PPAOS), the brunt (but not the only locus) of cortical pathology is in the premotor and supplementary motor areas of the left or left greater than right hemisphere. For example, in a study of 17 patients with a diagnosis of PPA or PAOS (Josephs et al., 2006), in which 11 patients had AOS, the premotor and supplementary motor cortex were the main cortical regions associated with AOS; all 11 AOS patients had autopsy findings consistent with corticobasal degeneration, progressive supranuclear palsy, or Pick’s disease, and tau biochemistry, while 5/6 cases without AOS did not have tau biochemistry. A recent study of 12 patients with PPAOS and no evidence of aphasia confirmed that the brunt of the pathology on neuroimaging is in the superior premotor and supplementary motor area (Josephs et al., in press). When accompanied by aphasia, cortical abnormalities tend to extend into the left posterior inferior frontal gyrus and anterior insula (Josephs et al., 2010; Ogar et al., 2007).

HOW MIGHT PAOS CONTRIBUTE TO THE UNDERSTANDING OF AOS AND REFINEMENT OF DIAGNOSTIC CRITERIA?

The careful study of PAOS may help refine diagnostic criteria and improve our understanding of AOS in general from several perspectives. We provide a few examples here to support this suggestion. They are related to: the anatomic underpinnings of the disorder; the evolution of the disorder; the possibility of AOS or PAOS subtypes; issues related to programming of speech versus nonspeech oromotor movements.

First, because the loci of abnormalities in PAOS do not follow a vascular distribution, the components of the motor programming network that break down, or are preserved, may be different than for stroke-induced AOS. As a result, some clinical manifestations may differ between the two etiologies. Shared AOS speech characteristics would provide additional support for diagnostic criteria developed from study of stroke-induced AOS. Differences might broaden diagnostic criteria for AOS in general, or require separate clinical diagnostic

criteria for each etiology. Features unique to each etiology could help identify a condition as vascular versus neurodegenerative and thus aid neurologic differential diagnosis. From a theoretical perspective, if there are differences in some of the clinical features of PAOS versus stroke-induced AOS, careful study of PAOS may open a window to additional ways in which speech programming processes might break down.

Second, whether or not PAOS has unique clinical features, longitudinal study of the disorder provides an opportunity to study the slow dissolution of speech programming, with possible insights into the relative vulnerability of various aspects of speech flow (e.g., rate, prosody, consistency) or speech units (e.g., phonemes, syllables, metrical units), and the ways in which the programming mechanism may respond, from a neuroplasticity perspective, to the gradual loss of its integrity.

Third, the study of PAOS may shed light on whether or not there are AOS subtypes, with distinct clinical features and/or neuroanatomic correlates, and presumably different underlying motor programming deficits. It has been suggested that breakdowns at different stages of motor programming, or lesions in different portions of the programming network, may lead to different types of AOS (Rosenbek, Kent, & LaPointe, 1984; Croot, 2002). The same questions can be asked about PAOS. Our current clinical impression is that there may indeed be subtypes of PAOS. We have now seen enough patients to suggest that some of the rate, prosodic, and articulatory differences among them cannot be explained solely by differences in severity or duration of illness. If this is confirmed, it will be clinically and theoretically important to determine if PAOS subtypes differ from subtypes of stroke-induced AOS. Any differences could further inform us about how speech programming can break down in different ways.

Finally, it provides an additional opportunity to examine the strength of the relationship between AOS and nonverbal oral apraxia (NVOA), and their disease course temporal relationship. AOS and NVOA emerge together with stroke etiology, but we know little about whether recovery from NVOA and AOS occur simultaneously or sequentially. NVOA occurs frequently but not invariably with PAOS (Josephs et al., 2010; Josephs et al., 2006; Josephs et al., in press). Further study is needed to determine if they can be completely dissociated, if one reliably emerges before the other, if they emerge simultaneously, and if their rate of decline is similar. Understanding these relationships may help clarify the degree to which speech production is directed by a modular control system, in which speech and nonspeech oromotor control are separable, or an overlapping or central speech and nonspeech control system (see Maas, Robin, Wright, & Ballard, 2008, and Ziegler, 2003, for a discussion of these hypotheses).

ADDITIONAL IMPLICATIONS

Investigation of PAOS is justified in its own right. Its recognition as a distinct neurodegenerative problem (particularly PPAOS), one that should not be subsumed under categories of PPA, may have important diagnostic, pathologic and treatment implications. In reference to PPA, Gorno-Tempini et al. (2011) have stated, “Widely accepted clinical criteria, likely supplemented by other biomarkers, will become essential in the coming years as a new generation of disease-modifying treatment options emerges” (p. 1007). This prediction can also be applied to PAOS. If clinical distinctions between PPAOS and PPA emerge as important for localization and disease diagnosis, then early identification of PPAOS would be crucial for early intervention with disease modifying (pharmacologic) therapies, when they become available. Even if differences between PPAOS and PPA are found to be unimportant for localization, clinical neurologic diagnoses, or underlying

pathology, the distinction will remain important for speech-language pathologists because aphasia and AOS do not respond to identical clinical therapy strategies.

It is important to recognize that our advocacy for studying PAOS does not imply that studies of AOS should group etiologies together. Until the similarities and differences between PAOS and stroke-induced AOS are more completely understood, we recommend that they be explicitly separated in both group and case series studies that include both etiologies and that the results be compared as a function of etiology.

CONCLUSION

There are convincing data that AOS can be caused by neurodegenerative disease. Although PAOS is accompanied and sometimes dominated by PPA, it can be the first or most prominent neurologic symptom and sign for an extended period of time, even over the full course of the underlying disease. It localizes to the left hemisphere, and when it is not accompanied by aphasia, the brunt of cortical anatomic damage tends to be in the premotor and supplementary motor areas of the frontal lobe. It tends to predict the eventual emergence of clinical neurodegenerative conditions with prominent motor manifestations, most often progressive supranuclear palsy or corticobasal degeneration, or with pathology consistent with those clinical conditions (i.e., tauopathy). Its careful study, especially in comparison to stroke-induced AOS, may have much to offer in refining clinical criteria for AOS diagnosis, and to our understanding of mechanisms for speech motor control and its breakdown in slowly progressive disease.

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