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Aphasia in Alzheimer's Disease and Other Dementias (ADOD): Evidence From Chinese

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Abstract

Speech and language impairments (aphasia) are typical of patients with Alzheimer's Disease and other dementias (ADOD) and in some pathologies are diagnostic e.g. Primary Progressive Aphasia (PPA). One question concerns the reliability and validity of symptomatology across typologically different languages. A review of aphasia in ADOD across languages suggests a similar pattern of word comprehension, naming and word finding difficulties but also evidence of language specific features in symptomatology e.g. processing of tone in Chinese languages. Given differences in linguistic impairments across languages, it is recommended that screening for aphasia in community and epidemiological studies use a Short ScreeningTest (SST) that can be delivered across dialects and languages in indigenous languages and also multilingual populations.

Keywords

bilingualism, cohort, speech therapy, public health, Greater Bay Area (GBA)

Dementia is a progressive decline of mental abilities that is accompanied by changes in personality and day to day behavior.[1] Defining features of dementia include: a) loss of memory, thinking and social abilities that are; b) severe enough to affect activities of daily living. Dementia is reported across cultures, languages and nations and methods of diagnosis including biomarkers, cognitive tests and clinical protocols are similar across testing environments resulting in some convergence in the prevalence and pathology of Alzheimer's Disease and Other Disorders (ADOD) such as Parkinson's Disease, Fronto-temporal dementia (FTD) and Primary Progressive Aphasia (PPA).[1-8] It is therefore tempting to assume that differences between cultures including access to education, language, literacy and other sociodemographic factors have no differential impact on prevalence of ADOD. This view is dominant in the literature despite evidence that cultural differences such as language and education might have differential effects on the emergence of ADOD across communities. For example, lower levels of education are associated with earlier diagnosis of dementia and speaking two or more languages is associated with a later diagnosis in some bilingual environments.[9,10] Therefore, it is an open question whether differences in culture and language impact on the presentation and prevalence of ADOD.

Aphasia and ADOD

A framework for dementia subtypes is given in Figure 1. In a majority of cases of ADOD, aphasia is eventually observed. Aphasia refers to the loss of spoken language or speech comprehension, reading and writing abilities due to brain damage which is due to neuropathology e.g. Alzheimer's Disease (AD). ADOD is caused by the deterioration of neural tissue accompanied by behavioral and functional decline including communication abilities. Neuropathology makes it likely that a brain network or region will suffer neurodegeneration and, because normal language function depends on a wide range of neural networks, ADOD will likely lead to some form of aphasia. It is not Alzheimer's neuropathology per se but the neural network affected that defines the symptoms of aphasia e.g. AD pathology will likely affect medial temporal lobes and associative areas initially so the presentation of AD may be characterized by episodic memory deficits before aphasia is later observed. Moreover, clinicians may observe language impairments clinically if Alzheimer's pathology affects a language network causing language specific symptoms. Other symptoms include loss of episodic memory, low self-esteem and depression.

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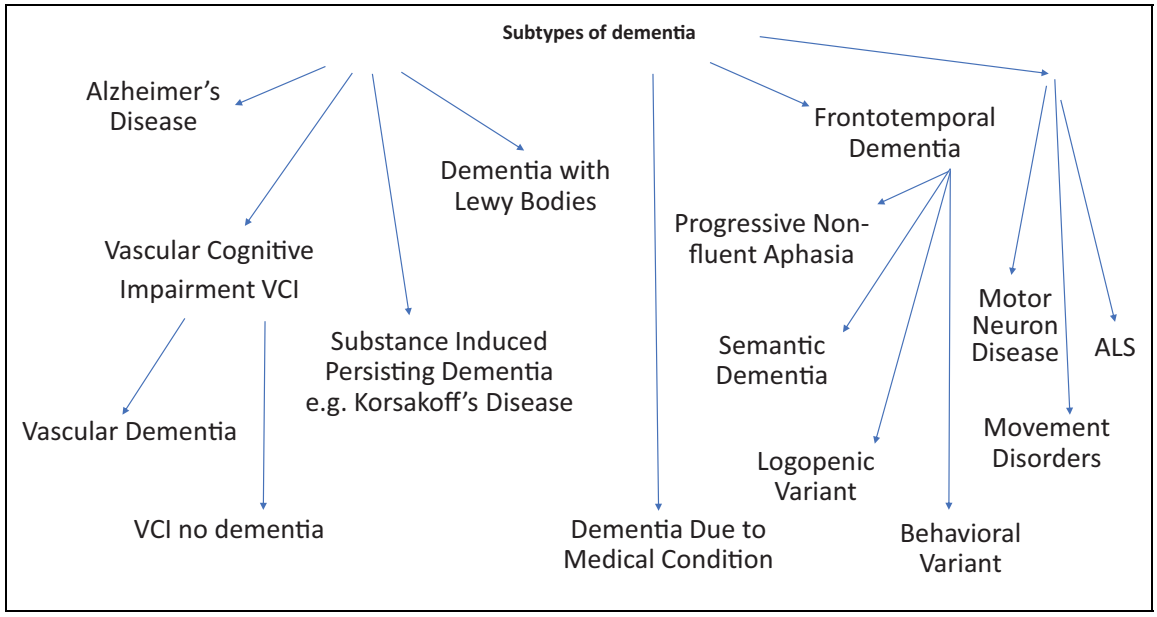

Figure 1. A framework for ADOD subtypes across cultures and languages.

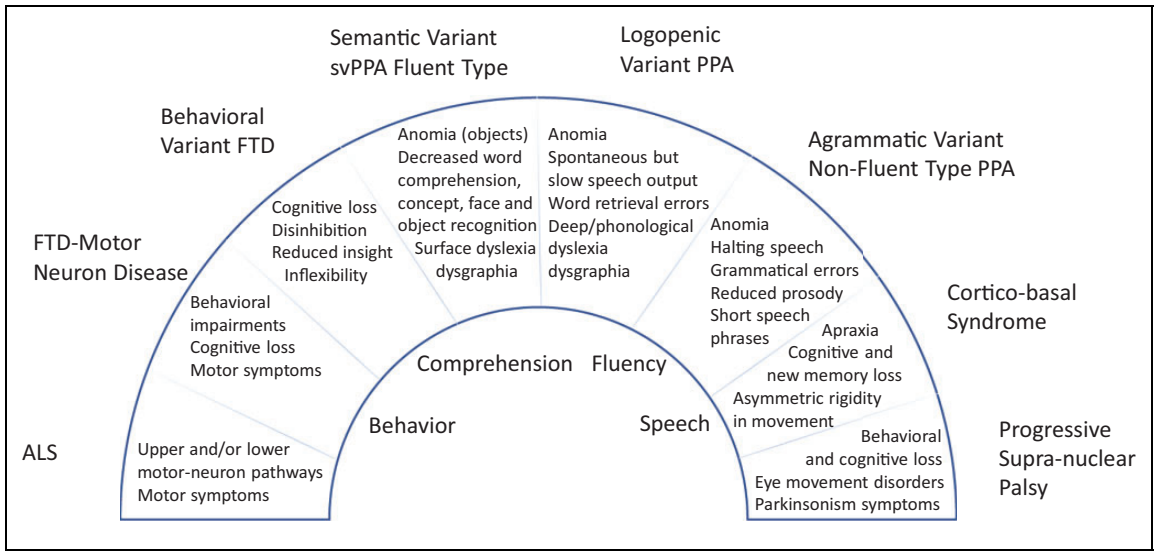

Figure 2. Spectrum of Fronto-temporal Dementia (FTD) characteristics including aphasia.

Aphasia is ubiquitous in ADOD at later stages of the illness and is characterized by impairments such as word finding difficulties called anomia. Whereas patients with Alzheimer's pathology are identified initially due to the loss of short term memory, most AD patients eventually suffer from anomia, as well as impairments to comprehension, speech, sentence recognition and reading and spelling/writing difficulties (called acquired dyslexia and dysgraphia respectively).[11] By contrast, aphasia is the initial diagnostic criterion for Primary Progressive Aphasia (PPA), which is a collection of language impairments that falls on a spectrum of FTD.[2-8] Aphasia in PPA includes subtypes with a variable pattern of symptoms at disease onset. The presentation of aphasia in subtypes of PPA varies according to behavioral and language dimensions such as comprehension, fluency and speech. These dimensions are depicted in Figure 2 as relative impairments across the FTD spectrum.

PPA subtypes are reported in a variety of Indo-European languages.[2-8] One question concerns the reliability and validity of PPA symptomatology across typologically different languages such as Chinese. One possibility is that aphasia in PPA shows a common pattern of comprehension, naming and word finding difficulties regardless of typological differences in grammar, prosody and tone. The alternative hypothesis is that such linguistic differences impact on symptomatology. There is a lack of cross-linguistic assessments for aphasia in PPA

despite evidence of language specific deficits following stroke in typologically different languages such as Chinese. Such evidence highlights potential diagnostic differences for PPA across languages although the research base is very underdeveloped. Similarly, assessment of PPA in minority environments including indigenous language users without access to health care as well as bilingual/multilingual speakers is a clinical issue.

Two reviews have compared the features of aphasia in ADOD including PPA across languages.[9-10] The reviews include case studies of patients who speak languages that are widely spoken globally (e.g. Chinese, Italian, Portuguese, Spanish). Less is known about understudied minority languages, or bilingual speakers and multilingual speakers from diverse language groups in large population cohorts (e.g. India). Indeed, in Greater China there are many minority language groups who do not speak standard Chinese (Putonghua) but of course do suffer aphasia. Similarly, in countries such as Brazil there are multiple languages spoken by indigenous populations but there are few suitable tests available to assess aphasia in these languages.

The features of aphasia in PPA summarized in Figure 2 are assumed to be similar across languages in terms of comprehension, fluency and speech. This is reflected in the use of diagnostic tests that are almost always translations of tasks that were originally designed for native speakers of Indo-European languages. Differences in grammar, prosody and syntax across languages are glossed over in these reports. This limits detection of language specific features in PPA and thus questions the reliability and validity of the diagnosis. Nevertheless, reports of PPA symptoms across multiple languages are emerging as clinicians become more aware of PPA diagnoses.[9-10] The symptoms range from impairments in fluency, confrontation naming of pictures (actions and objects), comprehension, repetition, reading and writing (dyslexia and dysgraphia).[10,12-27] If the features of PPA shown in Figure 2 are compared directly across languages, many diagnostic criteria are satisfied suggesting that cultural and linguistic differences are not relevant to the diagnosis of PPA.[10,12-27] However, this could be a false conclusion given that translation of tests developed for Indo-European languages may lead to under-reporting of language specific PPA symptoms. This is likely most problematic for tests of grammatical processing and literacy wherein the unique linguistic features of syntax and writing may reduce the reliability, sensitivity and validity of PPA diagnoses across languages.[17] Understanding PPA across languages therefore requires more than translation of extant tasks. Ideally, a native speaker can be recruited to administer tests of PPA but even bilingual clinicians may not be able to translate linguistic criteria into the native language. Even if a well-trained linguist is also recruited, it is challenging for a bilingual clinician to capture PPA symptoms across languages based on extant tests.[17-27] Moreover, in practice this is not always feasible.[6]

Development of a comprehensive assessment for PPA in any one of the thousands of languages spoken globally is a long-term process. This presents a conundrum for clinicians and researchers trying to identify communication difficulties in patients who have ADOD including PPA but who do not speak a language that is well documented. In clinical terms this is problematic because PPA is expected in any language and yet diagnosis and rehabilitation of language impairments will be delayed as comprehensive assessments are slowly developed. In research terms, it is desirable to identify communication disorders at an early stage in order to document the functional impairments of patients in large epidemiological and longitudinal studies so as to secure resources for early identification and, hopefully, prevention of language impairments in PPA.

Although it is ideal to test patients using validated instruments that are sensitive to the linguistic varieties of PPA in the clinic, the reality is that cognitive screening tests are the most readily used instrument in practice. This is evident in the widespread adoption of short screening tests of cognitive function such as the Mini-mental State Examination (MMSE) and the Montreal Cognitive Assessment (MOCA). Both instruments have been translated into different languages and validated in a large number of countries including in Greater China.[28] By contrast, screening tests for aphasia are lacking in most languages and this delays the identification of communication disorders in ADOD and PPA. From a clinical perspective, this impacts on the administration of speech therapy when it is warranted and, in the case of PPA, this may lead to an underdiagnosis of symptoms listed in Figure 2. If language impairments can be identified alongside cognitive impairments, the clinician is able to make a more informed recommendation about more comprehensive language test batteries that can be administered in a controlled testing environment. Such tests will require specialized knowledge of the native language that are informed by linguistic theory rather than translations of tests derived from other languages.[29]

Adding to this lack of resources is the need to develop a screening instrument that can detect communication disorders in a comparable way across linguistic environments. Given that the diagnosis of PPA relies on linguistic features that might differ across languages, a more productive strategy clinically would be to assess speech comprehension and production using a set of minimal functions that can be elicited in a variety of settings and in any language (see Figure 2). A short screening test for these functions that can be administered by a native speaking clinician would allow the detection of probable communication impairments in the context of recognizing features of the native language that are impaired. Ideally, the screening test would be administered by a speech pathologist who has had training in linguistics, thus allowing insights into the unique features of aphasia in their own native language. However, speech pathologists and therapists are not usually the first point of contact for patients who have ADOD or PPA in a clinical setting. Neurologists, psychologists and psycho-geriatricians are more likely to administer screening tests. Given that early detection of symptoms is vital, a short screening test of aphasia conducted in the native language of a patient is most likely to identify symptoms of PPA at first presentation. This could then

inform more specialized language testing of aphasia using comprehensive batteries after initial diagnosis.

Cross-Linguistic Assessment of Aphasia

Cross-linguistic assessment of aphasia is better developed for neurological conditions such as stroke. Such tests are typically comprehensive but also lengthy, and may not be well suited to the screening of PPA. Although tests designed for stroke patients in multiple languages have been used to detect communication difficulties in ADOD, cross linguistic comparison of aphasia in PPA lags behind. It is not straightforward to repurpose extant tests for stroke to identify the communication impairments in PPA. Translations of tests for aphasia such as the Boston Diagnostic Aphasia Examination; Western Aphasia Battery; and PALPA are widely used clinically. However, these tests are not always sensitive to language specific symptoms in typologically different languages—e.g. the PALPA in Chinese.[23-25] These tests might be valuable for the planning of cognitive rehabilitation and speech therapy in the native language of a patient. However, it is more desirable to assess linguistic domains in the native language that are known to detect PPA across languages. For example, fluency is a widely validated dimension that can be used to discriminate different forms of PPA that reflect different lesion locations e.g. fluent and non-fluent aphasia. Comprehension, confrontation naming and literacy are also sensitive tests for PPA as shown in Figure 2. A focus on these domains is likely to detect PPA across languages even using a short screening test of aphasia. This is not to underestimate the importance of comprehensive language specific tests of aphasia in PPA. These might be sensitive to unique neuropathological characteristics that are only revealed with language specific tasks. Unfortunately, such tests are not available for the majority of languages. A short screening test for aphasia that includes the domains summarized in Figure 2 is therefore recommended. One advantage of developing a short screening test for aphasia is that a wide range of researchers can be trained to administer the test efficiently in large epidemiological studies.[28,30-35]

PPA Across Languages

Given the diagnostic importance of communication difficulties in ADOD, the characteristics of PPA in different languages have become more relevant in clinical research globally. PPA has been reported in multiple languages ranging from Indo-European to Sino-Tibetan. However, cross-linguistic studies are mostly single case reports of bilingual and multilingual speakers. In recent reviews of cases for whom English is a second language (L2), symptoms also appeared in the first language (L1) including for Brazilian Portuguese, Catalan, Chinese, Cypriot Greek, Czech, Dutch (Flemish), Farsi, Finnish, French, Friulian, German, Greek, Gujarati, Hebrew, Hindi, Hungarian, Italian, Japanese, Korean, Norwegian, Polish, Portuguese, Romanian, Spanish, Swedish, Turkish, Ukrainian and Welsh.[9-10] Of diagnostic interest, indicators such as speech output, word finding, semantic knowledge and comprehension difficulties, repetition, reading and writing impairments are often earlier in onset in L2 even if L2 is the dominant language used in daily life—although eventually language deterioration becomes equivalent in both languages. Tests of grammatical processing are rarely reported, reflecting the language specific nature of grammar and syntax.

Word-finding is the most frequent *first reported symptom* of PPA across languages, and therefore a target for developing cross-linguistic assessments.[12-16] However, word finding is a blunt indicator since all patients with ADOD ultimately present with word finding deficits. Information on grammatical processing is lacking from case reports likely due to difficulty when matching equivalent tests in different languages using different syntactical constructions. However, there are reports of grammatical deficits in both languages of bilingual speakers with PPA including Brazilian Portuguese, Japanese and Hungarian.[17,18] There are also reports of acquired dyslexia and dysgraphia in single cases with similar features.[19-27] It is therefore desirable for clinicians to develop tests that are sensitive to differences between languages and yet can be applied across linguistic environments for the assessment of PPA. Given consensus criteria for PPA, it is important that diagnostic tests are *equally* sensitive across languages and also allow for linguistic nuances as developed in cross linguistic assessments for aphasia after stroke.[36,37] However, this is not typical of comprehensive screening tests for PPA or consensus criteria for diagnosis of PPA.[11,38-40]

Linguistic Diversity

To improve diagnostic sensitivity of PPA across languages, it is necessary to understand reported differences in PPA across languages. Some of the diagnostic features in Figure 2 reflect linguistic properties that are not found across all language groups e.g. surface dyslexia in Turkish and phonological dyslexia in Chinese. One approach to improving diagnostic validity would be to reclassify diagnostic criteria in PPA according to language specific features. Functional criteria such as fluency, comprehension, grammatical processing and literacy can be assessed in any language but symptomatology will be language specific. This is not a trivial recommendation since a lack of linguistic adaptation may lead to misdiagnosis, and in the worst case, under-diagnosis of patients who speak uncommon or less well documented languages. However, this strategy is expensive, resource intensive and slow.

Despite this cost, the effort may be necessary. Linguists generally agree that language specific "surface" differences (either spoken and written) converge on "deep" processes that are shared across all languages. Despite this *universality* assumption, there is evidence from cross-linguistic studies of aphasia in stroke that surface differences do emerge in speech pathology and symptoms of language impairment in aphasia are distinctive across languages.[29,41-44] This is also observed in case reports of PPA.[45] However, one challenge in comparative research on aphasia in PPA is a lack of comparable assessment

tools and outcome measures that can be used across different languages for clinical and research purposes. A related question is whether surface features benefit from language specific treatment once PPA is diagnosed.

A different approach is to develop standardized tests representing shared linguistic features. For example, the Comprehensive Test of Aphasia (CAT) has been adapted into multiple languages.[27] Versions are available in Basque, Catalan, Croatian, Cypriot Greek, French, Greek, Hungarian, Norwegian, Serbian, Spanish, Swedish and Turkish i.e. all European languages. The CAT contains both comprehension (subtests 7 to 11) and expressive language tests (subtests 12 to 27) that measure a wide range of fluency. The results show that linguistic properties have different importance across languages. For example, morphological complexity is relevant in highly inflected languages such as Basque, Greek and Spanish, whereas spelling-sound regularity of orthography is more important in less transparent orthographies such as English and French. One recommendation is to find items and linguistic structures related to underlying pathology that are comparable across languages. Furthermore, using the same number of subtests, tasks and items as well as the same scoring criteria facilitates comparison between testing sites and allows for cross-linguistic investigations.

So far, the diagnosis of aphasia in group studies of ADOD and PPA in non-English language environments is limited to the translations of tests first developed for English speakers with some adaptations for local languages. For example, in a large scale study of 100 patients from Brazil, the assessments included fluency in spontaneous speech and on the Boston Cookie Theft Picture Description Task (for the assessment of grammatical production); syntactic comprehension evaluated through matching tasks (sentences-pictures) from the Beta MT-86; semantic comprehension evaluated through word-picture matching and word definition tasks from the Semantic Memory Battery; object naming and sentence repetition using items from the Boston Diagnostic Evaluation and Boston Naming Test; and literacy using reading aloud and dictation tasks from the HFSP protocol[20] and Beta MT-86 aphasia protocol (both developed primarily for European languages).[45] However, as with the CAT, these tests do not always translate easily into non-European languages such as Chinese and also do not always reflect cultural and linguistic uniqueness in language typology. The lack of comprehensive cross-linguistic assessment tools developed for PPA thus hinders the comparability of diagnostic validity across languages for clinical and research purposes, and therefore management of multilingual individuals with PPA. This is compelling since, by some estimates, bilingual and multilingual speakers make up half the global population.[46,47]

At least one fifth of multilingual speakers can be found in Greater China wherein indigenous (minority) languages are common even though the official "common" language is Mandarin (Putonghua). Greater China also has the largest number of potentially undiagnosed cases of ADOD (including PPA) in the world and these cases are only now presenting to the clinic for diagnosis after decades of neglect. Epidemiological studies suggest that the number of cases of ADOD in China has been severely underestimated due to the low income status of the country before the 21st century. Another impediment to accurate diagnosis has been the lack of reliable and valid cognitive and language assessments that can be used to detect aphasia and cognitive decline in Chinese speakers. This situation is improving after nearly 50 years of research in Hong Kong, Singapore and Taiwan. However, it is still a challenge to find a reliable and valid sShort sScreening Ttest for aphasia that is suitable for use throughout Greater China including the Greater Bay Area.

An effective Short Screening Test (SST) needs to be a) compatible with internationally standardised epidemiological research methods i.e. the test can be administered to hundreds of thousands of people by health care workers who are not trained linguists or speech therapists; b) the duration of testing must be short—no more than 15 minutes; and c) sensitive to aphasia in multiple languages (dialects). More importantly, the test must be administered in the native language for more than half of the sample in Greater China and that could include over 100 different languages in several remote parts of the country. The test should be administered by a native speaking health care worker in local communities but the patterns of aphasia identified must also be comparable using a set of minimal PPA criteria so that an estimate of the prevalence of communication difficulties could be included in epidemiological reporting of PPA throughout the country. There are currently standardised tests of aphasia available for only 2 or 3 Chinese languages (Cantonese and Putonghua) and these are designed primarily for use with stroke patients. There are some examples of testing matierials designed to assess PPA in Chinese in the Greater Bay Area.[81-82]

Dementia in Greater China

Populations around the world are rapidly aging and Greater China has the largest number of probable future cases with an estimated 500 million people over the age of 60 by 2050. The number of people with ADOD is estimated to be 9.19 million and the number in the Greater Bay Area is 5.69 million in epidemiological studies.[30-32] A majority of cases will be multilingual, often speaking Standard Chinese (Putonghua) as a second language. There is no prevalence data reported for PPA in Greater China. Indeed, relatively little is known about the characteristics of communication disorders in ADOD in Chinese speakers at all.[33,34,28] Most reported findings have been epidemiological or radiological with far less attention to communication disorders.[35,48-53] For Chinese speakers with ADOD including PPA, a handful of case studies suggest that patients present with language impairments reported in other languages—specifically difficulties with word fluency, processing action and object pictures and acquired dyslexia.[54-61] However, the patterns of aphasia are not always identical to the symptoms reported in patients from other cultures.[62] There will of course also be cultural and linguistic differences *between* Mainland Chinese speakers with ADOD who speak different

dialects and languages. Cultural differences should not impact on the prevalence of dementia, risk factors or symptomatology across linguistic environments in principle. However, because China is now a low to middle income country, there will are differences in socio-demographic factors that may impact on performance using tests translated from Indo-European countries, thus reducing the reliability and validity of accurate diagnoses. For example, a large proportion of the elderly population is *illiterate* (48.3%) and the number of people above age 60 who have *no formal education at all* is among the highest in the world. Not surprisingly, the rates of health literacy are low at 4.7% and the proportion of basic health skill and chronic disease prevention awareness is also very low at 3.8%. Due to the one-child old policy, the proportion of adults without children is rising. The number of empty nesters is now relatively high, with nearly 50% in urban and 40% in rural locations. These characteristics are particularly problematic for patients with ADOD who have communication difficulties as they are isolated and without social interaction, support and income. Furthermore, long-term care and palliative care, speech therapy and rehabilitation are not always covered by health insurance nationally and expenses are paid by patients themselves. Only affluent cities (Beijing, Qingdao and Shanghai) reimburse costs of long-term and palliative care. Therefore, the burden of aphasia and other communication disorders in Greater China is at a critical stage and increasing.

In an ongoing study with 25,000 individuals, Qi et al., (2018) analyzed the variables that discriminate ADOD from healthy aging in seniors aged over 60 years.[33] Qi et al found that people with ADOD in Mainland China: 1) have a relatively high life expectancy compared to other countries but this is lower than for other Western Pacific Regions including Australia, New Zealand and Japan; 2) have multiple communication difficulties including hearing (29.3%) and speech (14.5%) impairments; 3) low levels of health literacy (<3%); 4) high levels of illiteracy (48.3%); 5) low levels of primary care and treatment particularly for females in rural areas; and 6) a high percentage of unmet needs due to poverty (69%). When comparing the risk factors that distinguish between ADOD patients and healthy controls, they identified standard biomarkers that increase risk for ADOD e.g. apolipoprotein E (ApoE), asthma, diabetes and stroke. However, uniquely, they also identified variables that significantly mitigate the expression of risk into ADOD including 1) higher levels of formal education; 2) literacy; 3) exercise; 4) playing games (Mahjong); 5) neighborhood interaction; 6) social conversation; 7) reading newspapers; and 8) tea drinking. Some of these factors e.g. low levels of education, exercise, social interaction are well known to be risk factors for patients with ADOD from other countries whereas other factors (mahjong and tea drinking) are more culturally specific. In preliminary analyses, we have found that speaking more than one dialect does not distinguish ADOD patients from healthy controls - although we note this may be outweighed by correlations with low levels of education, literacy and lack of social engagement in ADOD patients tested to date. Overall, it is advisable for seniors who at risk of ADOD in Mainland to manage their lifestyles by engaging in social interventions that promote communication, conversation and social engagement to retain brain health and reduce the risk of ADOD. This is also true for Chinese speakers with diagnosed ADOD. However, because we expect language impairments in seniors who have ADOD including PPA, it is recommended that assessment of probable ADOD in Mainland Chinese patients includes short tests of speech comprehension, production, written word recognition and production, in addition to other cognitive or sensory impairments. This is being included in our current epidemiological studies in the Greater Bay Area including Hong Kong.

Table 1. Evidence of Language Impairments Reported in Chinese Speakers with Aphasia.

Domain	
Fluency	Chao et al, 2013[64]*; Filley et al, 2006[65]*; Kong 2011a:b[62,63], 2009[66]†; Kong & Law, 2004[67]†; Liu et al, 2015[52]*; Liu et al, 2018[68]*; Gorno-Tempini &Tee, 2019[61]*
Naming	Arévalo et al, 2011[69]†; Crepaldi et al, 2012[70]†; Weekes & Chen 1998[44]†
Repetition	Dong et al, 2017[50]*; Weekes et al, 2012[26]*; Weekes & Luo, 2004[71]†
Grammar	Law & Leung 2000[72]†; Law 2000[73]†; Leung 1998[74]†; Wang et al, 2016[75]*
Meaning	Bi et al, 2007[60]*; Weekes 2000[23]*; Zhang et al, 2008[76]*; Zhou et al, 2013[53]*
Reading	Bi et al, 2007[60]*; Ting et al, 2013[57]*, 2016[58]*, 2018[59]*; Weekes 2000[23]*; Wu et al, 2015[77]*
Writing	Law, 2001[78]†; Law et al, 2005[79]†; Leung et al, 2012[80]†; Yin et al, 2005[81]†

*denotes evidence from ADOD patients †denotes evidence from stroke patients.

The remainder of this review will highlight the features of aphasia in Chinese speakers with ADOD that we expect to observe in our future studies so that communication impairments can be detected early - thus allowing prevention of further functional decline and encouraging patients and care givers to become more socially engaged with functional communication via speech therapy particularly for PPA. The data reported so far shows similar patterns of aphasia in Chinese but also some culturally specific linguistic differences in ADOD that need to be accommodated in future screening tests.

Chinese Languages

Chinese "dialects" are widely spoken languages worldwide - not only in the Sino-sphere of Mainland China, Hong Kong, Macao, Malaysia, Singapore and Taiwan but also in many other countries. Therefore, reports of aphasia will increase. For example, in the US, it is estimated that up to 40,000 Chinese speakers have some form of language impairment already.[63] Assessment tools for aphasia in Chinese speakers are available for stroke patients, and these may be suitable for patients with ADOD including patients with PPA, but this requires far greater research resourcing. Reports of aphasia in Chinese that

reflect the linguistic domains relevant to dementia are summarized in Table 1. It can be seen from Table 1 that reports of aphasia in stroke are long standing but reports of aphasia in dementia have a more recent history. For both dementia and stroke patients, the literature is dominated by case reports reflecting a lack of resources.

Chinese languages differ in terms of linguistic features including speech, orthography, phonetics, and grammar. All Chinese languages are syllabic, tonal and use logographic writing systems (simplified and traditional characters). In contrast to alphabetic writing systems, there are no letters or symbols (graphemes) to represent phonemes in Chinese languages. Even more challenging for assessment of aphasia, the many Chinese "dialects" differ significantly from one another in syllable pronunciation, assignment of syllable tone and vocabulary i.e. Chinese languages are not mutually intelligible making it misleading to assess Chinese language impairments in one language only.[62,63,66]

Law, Kong and colleagues have written extensively about the unique linguistic features of Chinese that are relevant to the assessment of aphasia after stroke and head injury. Curiously however, they have not yet explicitly considered ADOD or PPA in their analyses. According to Law and Kong, Chinese languages are completely unique in terms of their linguistic characteristics. For example, when compared to Indo-European languages, Chinese is analytic i.e. without inflectional or derivational morphology. Grammatical meanings are often conveyed using word order, adverbs, grammatical particles such as aspect markers or sentence final particles and these can be highly variable in discourse. Chinese also permits omission of subjects and objects if they can be understood from context. For example, elliptical sentences that can signify aphasia in some languages can be considered correct and entirely grammatical in Putonghua (common Chinese), especially in connected speech and conversations. Given linguistic differences, it is not recommended to translate tests of aphasia between Chinese for diagnosis of language impairments in ADOD or PPA. Assessment of aphasia in Chinese requires selection and modification of relevant linguistic dimensions in relation to cultural standardization (dialect) and this extends to tests of cognition and memory particularly in Mainland China where education and levels of literacy are low in seniors over the age of 60 years.[82,83]

Standardized tests for the assessment of aphasia are readily available due to the work of Law and Kong. These include the Mandarin version of the Boston Diagnostic Aphasia Examination (M-BDAE) and Cantonese version of the Western Aphasia Battery (CAB). Both batteries contain translations of subtests for auditory comprehension, verbal expression, fluency, naming, repetition, reading, and writing and are widely used in Taiwan and Hong Kong for the assessment of stroke patients. The Bilingual Aphasia Test (BAT) can also be used to test Chinese-English speakers. Fluency can be assessed using elicitation tests that require sentences to convey a narrative. Elicitation tasks include describing single or sequential pictures, reporting events, telling or retelling stories. Cross-linguistic studies using culturally inappropriate pictures, topics, or stories have been shown to affect the validity of the assessment however. For example, "Cinderella" fails to elicit discourse from Chinese speakers. Use of culturally inappropriate stimuli in ADOD patients may result in overestimation of aphasia due to lack of relevant content.[63] Instead, a native speaking multilingual clinician should estimate fluency any noting nuances in melody, prosody, phrase length, rate of speech, grammaticality, effort, articulatory precision e.g. tone in simple conversation. For example, recalling events of the previous day or biographical details of the patient in narrative forms rather than answering questions with complicated syntax that can vary between Chinese dialects.

Aphasia in Chinese Speakers With ADOD Including PPA

Compared with reports of aphasia in Chinese speakers after stroke, there is a paucity of standardized assessment tools for the Chinese population with ADOD and hence a lack of published studies. One exception is acquired dyslexia and dysgraphia in ADOD.[81,84] There are detailed reports of bilingual Chinese-English speaking cases who have ADOD or PPA. Bilingual clinicians working in Hong Kong have developed resources for testing bilingual or multilingual speakers of Chinese. However, most research is with Cantonese dominant speakers and therefore investigations in different Chinese dialects are currently lacking.[63]

Chinese speakers with ADOD are reported to have language impairments as summarized in Table 1 including reduced fluency, confrontation naming, repetition and reading—primarily lexical tasks. Deficits in grammatical processing are not as well documented possibly reflecting the difficulty translating English grammar into Chinese. Similar to English speaking cases, Chinese PPA patients do show a reduced capacity to name objects and actions and they produce reading errors that have been likened to surface dyslexia in English and in Japanese.[85-87] Some studies also suggest specific difficulties with the processing of tone in comprehension and production tasks.[61] Interestingly, Chinese speakers with aphasia following stroke show a pattern of oral reading errors that substitute the character tone in oral reading or so called *tonal dyslexia*.[71] This may be a diagnostic feature of PPA in Chinese. However, this hypothesis has not been tested in ADOD patients to date.

According to Table 1, testing Chinese speaking patients with ADOD (and in particular PPA) should include measures of spontaneous speech documenting discourse content, syntactic and phonological aspects of the Chinese language, word-finding, semantic processing, word comprehension, confrontation naming, and literacy - specifically tests for acquired dyslexia (deep, surface and tonal). Additional tests of nonverbal semantic memory, autobiographical memory and visuospatial skills are also recommended for differential diagnosis as well as neuro-radiological tests of frontal and temporal lobe atrophy and/or hypoperfusion.[82,83] It is important to highlight that reports of PPA in Chinese are anecdotal at the present

time. Case report data is not sufficient to claim that PPA has diagnostic validity in Chinese speakers at this preliminary stage. However, the evidence does suggest that testing patients who have probable dementia on domains listed in Table 1 will reveal cases of PPA.[82,83]

Some of the reported evidence of Chinese speakers with PPA suggest that language specific measures of reading and writing may be justified. Tests of literacy in Chinese are plentiful, standardized and already well established in the literature on aphasia after stroke and childhood dyslexia. Tests are therefore readily available for clinicians to assess acquired dyslexia and dysgraphia. One question for future studies is whether acquired dyslexia manifests differently in Chinese speakers with PPA compared to PPA in Indo-European languages. Mandarin speaking patients who have PPA in Singapore (a multilingual linguistic environment) show an unexpected tendency to produce a pattern of semantic reading errors referred to as deep dyslexia in Indo-European languages.[57-59] Deep dyslexia is not typically found in PPA in these languages wherein phonological and surface dyslexia or dysgraphia are more commonly reported.[88] There is evidence that Chinese speakers with PPA present a mixture of deep and surface dyslexia suggesting a heterogeneity in symptoms possibly due to the complexity of the Chinese writing system.[56] It is important to note that studies of acquired dyslexia and dysgraphia are likely to have implications beyond clinical diagnosis including understanding the neurobiology of language.[81,84] Studies of PPA patients in several languages has contributed to the development of theoretical models of reading and writing.[85-87] Studies of Chinese PPA cases PPA may have a similar impact.[76,77]

Measures of speech fluency in Cantonese speakers can be elicited using standardized formats recommended by Kong and Law following research studies with patients who have stroke or head injury. One of these tests is the Cantonese Linguistic Communication Measure (CLCM). The CLCM uses indices that evaluate contents such as lexical diversity and counts of informative words and errors; grammatical support; degree of elaboration; and efficiency such as rate of producing informative words.[67] The Quantitative Production Analysis uses a storytelling task to elicit language samples.[78] It contains detailed procedures for extracting narrative words in Chinese and classifying words into Chinese parts of speech. It also includes sensitive criteria for analyzing Chinese compound words and degree of embedding, such as the use of complex sentences and embedded clauses. Another established test of speech fluency is the Main Concept Analysis (MCA) which can be used to capture the presence, accuracy, and completeness of oral narrative content and production efficiency among Chinese speakers with aphasia.[66,62] An important characteristic of the CLCM and MCA is that the stimuli are culturally appropriate for Chinese speakers. Standardized tests of language in PPA for other Chinese dialects are currently lacking although some are in development.[61]

Table 2. Examples of Questions for Short Screening of Aphasia in Patients with Alzheimer's Disease.

Domain	Examples of questions and tasks for screening of language impairments in ADOD
Fluency	Describe a complex picture depicting a number of activities noting melody, prosody, phrase length, rate of speech, grammaticality, effort, articulatory precision e.g. tone
Naming	Present patient with uncommon items to name e.g. pictures of actions and objects
Repetition	Present nonwords and words (nouns, verbs) of variable length; sentences, phrases
Grammar	Present commands increasing in complexity "touch the desk before touching nose"
Meaning	Ask for definition of words increasing in complexity e.g. "point to something red now"
Reading	Ask to read aloud newspaper; words (exception and regular), sentences, nonwords
Writing	Ask to write sentence from dictation; words (exception and regular) and nonwords

Policy recommendations

Researchers have only just begun to develop the necessary tools to assess cognition, language and speech in Chinese speaking patients with ADOD in population cohorts in Mainland China.[82,83] Not surprisingly, little progress has been made in the study of PPA to date. It is therefore vital to standardize and implement reliable and valid tests of speech and language for this population and this must be a long-term goal of public health in the Greater Bay Area. In the meantime, extant tests of aphasia, language and speech that are designed for Chinese speakers who have had a stroke are available for use. However, these are not necessarily fit for purpose when diagnosing communication impairments in ADOD and are not specific enough to detect PPA in Chinese speakers at the present time. Similarly, tests designed for the brief screening of language impairments in stroke patients across languages have not been developed for Chinese or any other "Sinitic" language yet.[89,90] Those relatively short tests could be adapted to Chinese but this may not be the ideal solution for estimating the prevalence of PPA in Mainland China. At a minimum, there are major obstacles to overcome before simple translation of stimuli in those instruments could be recommended for the diagnosis of aphasia in PPA. The most critical problem is how to test syntax and grammatical processing using extant tests for Indo-European languages—including established tests such as the BDAE and the WAB. To give just one example, Chinese has no inflectional morphology unlike languages where PPA is well recognised. Chinese is also characterized by omission of topic and grammatical subjects in sentences and use of elliptical sentences. Nevertheless, grammatical impairment can be observed in the disruption of morphological and syntactic structures in Chinese speakers after stroke and therefore prima facie in PPA. One possible pattern is the disruption of grammatical judgment; another is the acquired loss of prepositional co-verbs and utterance-final particles; and another is patients who have

impairment with the production of aspect markers without a difficulty producing closed class words.[63] In bilingual Chinese-English speakers, sentence production can be impaired in both languages but manifest differently i.e. the ability to construct sentences at the clause level and the use of morphological structures can be more disrupted in Chinese than in English.[80] One consequence of *such language specific features* is that patients might "grab" the linguistic devices of the native language to communicate producing "mixed aphasia". Thus, Chinese PPA patients may use aspect markers for discourse to improve fluency particuarly if they are bilingual or speak more than one dialect. The implications for diagnosis of PPA are to focus on a brief screening for multiple domains of functional language use as described in Figure 2 i.e. comprehension, fluency, repetition, reading and writing. Given that testing will be performed in the native language and these are variable in China, the examiner should record the compensation strategies in all languages spoken.

A framework for the screening of communication difficulties in Chinese speakers who have dementia is summarized in Table 2. Critically, this table is based on evidence from case reports of aphasia in patients with neurological damage including ADOD, PPA and stroke and so it provides a guide to the most likely communication disorders in Chinese but does not yet form the basis for a standardized battery of tests for diagnosis of PPA or other pathology. It is certainly not the case that the research base is sufficient to warrant consensus criteria for Chinese speakers yet. However, with the increasing demand for screening of language impairments in large cohorts of patients who have dementia, it is possible that some patterns of aphasia may emerge that are diagnostic of PPA. This awaits investigation. In the meantime, the SST for Chinese speakers that is currently under development could give a basis for research on reliability and validity of criteria as demonstrated in other language impairments.[36]

In view of the growing demand for the clinical assessment of communication impairments in Mainland China and the lack of any standardized protocol for assessing aphasia in suspected PPA cases, it is recommended that testing includes the SST for identifying language impairment in all cases of probable dementia. The most relevant language functions are summarized in Table 2 although this is not an exhaustive list. It is recommended that these domains are tested in studies of dementia including PPA in Mainland China, Hong Kong, Singapore, Taiwan as well as in international linguistic environments with a large diaspora of Chinese speakers. The advantage of using the SST to assess fluency, comprehension, repetition, reading and writing is that the clinician can administer tests at the "bedside" and home visits that are characteristic of epidemiological studies. The screening questions are relatively routine and a natural part of the discourse in a testing situation, noting that, because patients with motor deficits are common in FTD, the execution of commands could limit assessment in some cases. The identification of language and speech deficits can then point to more advanced testing by a trained speech pathologist.

Tests for the detection of aphasia in Chinese speakers that are sensitive to fluency, comprehension and syntactical processing are available and could be administered as a validity check for the SST. One example would be the Northwestern Anagram Test (NAT) which has been used with Chinese speakers who have Broca's aphasia following stroke.[64] Another example is the Test for the Reception of Grammar TROG that has been translated into other languages.[17] Indeed, several tests have been developed specifically for grammar and lexical processing in Chinese speakers and these can be used to validate results of testing using the SAT in large scale epidemiological research.[64,65,68,70,72-77,80] This research is currently underway in Hong Kong.

Summary

The intention of this review is to highlight the communication difficulties of Chinese speakers who have ADOD. It is not intended to propose diagnostic criteria for PPA subtypes in Chinese, although the reviewed studies do point to a number of possible *language specific tests* that can be developed. The outcome of the review is to recommend a short screening test to detect significant communication, language and speech difficulties of Chinese speakingcases in epidemiological studies, bearing in mind that such studies do not allow the comprehensive assessment of subtypes of PPA at this stage. The evidence base points to the use of functional tests of communication skills that may be useful for the development of future research studies of PPA in Chinese speakers. However, the literature is too shallow and contains no more than impressionistic findings from single case studies. Some findings do however point to linguistic aspects of aphasia in Chinese speakers that may become diagnostic following testing in larger samples with better control over correlated variables such as differences in bilingualism, cognitive status, education, literacy and socioeconomic status. One issue in the Greater Bay Area is the lack of trained professionals who can provide speech therapy. Speech therapists are available in affluent parts of Greater China (Hong Kong), Taiwan, Singapore and in non-Chinese speaking countries. However, for most patients with ADOD in Mainland China (Guangdong), these services are not readily available. The rationale for including the SST in future studies is to extend the breadth of information about ADOD in combination with cognitive screening tests already validated for use with Chinese speakers (MOCA, MMSE and the Oxford Cognitive Screen). This does not preclude development of language specific batteries by speech therapists in due course.

It is anticipated that the SST will give the first evidence of communication difficulties and aphasia including PPA in our cohorts of patients currently under investigation in Mainland China includingseniors in the Greater Bay Area of Guangdong—with a total population exceeding 100 million people all dominant Cantonese speakers but critically also often speaking at least one other Chinese language (e.g. Putonghua). If the SST is able to isolate communication difficulties in patients who have dementia in Greater China, there is scope to develop

the test for other low to middle income countries with large populations that are also aging rapidly. The potential of the SST as compared to more comprehensive tests of aphasia designed for speech therapy is that the SST can be administered in any indigenous language in any part of the world. This would allow a greater number of cases who have communication disorders to be detected early and contribute to the UN Strategic Development Goal of Universal Health Care (UHC). Returning to the theoretical question posed at the outset of this review, it is not yet possible to support the hypothesis that linguistic differences impact on the symptomatology of PPA. This is due to the paucity of evidence of cross-linguistic assessments for aphasia in ADOD despite some evidence of language specific deficits following stroke in typologically different languages. Further studies that focus on the potential diagnostic differences in PPA across languages are required before the language universal hypothesis can be rejected.

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