Global Journal of Neuroscience Jan. 17, 2021, Vol 2, No 1

Global *Journal of Neuroscience*
2021; 2(1): 1-24.
ISSN Online: 0000-0000; ISSN Print: 0000-0000
Website: http://natureschol ars.com
Email: Glo_J_Neu@126.com
Publisher: Scholars Publishing, LLC

Review

Aphasia after Stroke: Updates into Overcoming The Diagnostic Dilemmas

Samwel Sylvester Msigwa[1,✉], Yan Li[1], Xianglin Cheng[1,2]

[1]Department of Neurology, The Clinical Medicine School of Yangtze University, The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei, 434023, China. [2]Department of Neurology and Rehabilitation, The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei, 434023, China.

✉ **Correspondence**
Samwel Sylvester Msigwa, Department of Neurology, The Clinical Medical School of Yangtze University, The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei, 434023, China. Email: neurovascular7@gmail.com. Telephone number: +86 13135752757.
Received: November 9, 2020; Accepted: December 2, 2020; Published online: January 17, 2021.
Cite this paper: Samwel Sylvester Msigwa, Yan Li , Xianglin Cheng. (2021) Aphasia after stroke: updates into overcoming the diagnostic dilemmas. *Global Journal of Neuroscience*, 2(1):1-24. http://natureschol ars.com/gjn.020101. https://doi.org/10.46633/gjn.020101.

Abstract

Aphasia after stroke (AAS) is a decline or impairment of language processing effected by an acquired cerebral lesion leading to significant consequences in all post-stroke phases. Stroke mimics may estimate for up to 1/3 of all critical stroke consultations, with estimated up to 26% and 43% false-negative and false-positive cases, respectively, hence, posing a hurdle to authenticate AAS's diagnosis. The new literature recommends a triad of questions to deliver during history in chronological order to tackle the diagnostic dilemmas. For AAS assessment, a quick aphasia battery emerges as a time-saving tool to administer in 20 minutes compared to most verified time-consuming tools for a language evaluation. Contemporary research authenticates Oxford cognitive screen as a relevant, fine-tuned screening tool for post-stroke cognitive deficits. Unlike the communication outcome assessment tool facing controversy, consensus regarding suitable tools for quality of life, emotional well-being, and language evaluation exist. Similarly, guidelines for the assessment of AAS-depression comorbidity prevail unestablished. We outlined the practical assessment tools proposed to serve this purpose. Future research is also obliged to appraise these tools in the acute care setting: detailed laboratory investigations and imaging modalities for AAS mimic exclusion covered in this review. However, neuroimaging is the cornerstone for the accurate diagnosis, classification, distinguishing AAS from the mimics, and rehabilitation prognostication.

Key words: Aphasia, Neuroimaging, Comorbidity, Cognition Disorders, Stroke, Referral and Consultation.

1. Introduction

Non-communicable disorders and stroke are the most prominent aetiologies of global mortality, pointing to >36 million deaths annually.

Furthermore, adding 14 million cases dying at a tender age <70 years, mainly in low-income middle-income nations, leading to significant economic impact (1-3).

Stroke is a dominant global etiology of fatality and disability, adding the economic burden due to post-attack treatment expenses (4). An increment has brought the growing trend of stroke in the youth population in classical risk factors, mainly hypertension (HTN), smoking, and illegal drug usage (5). For the past forty years, the stroke incidence duplicated in low and middle-income nations. Meanwhile, declining by 42% in high-income states (6). Similarly, in China, the Stroke burden has grown over the past three decades and remains exceptionally high in rural areas. There is a north to south gradient in China's stroke, with the most exceptional stroke load seen in the north and central provinces (7,8).

Communication impairment is prevalent throughout the inpatient stage of stroke care, yet medium therapy provision is lesser than the urged levels. The most popular communication difficulties following stroke are aphasia and dysarthria, which regularly coincide in up to 28% of the post-stroke cases, pointing to poor stroke recovery, especially in older cases (9,10).

Speech and language disorders are an umbrella term that applies to a spectrum of expressive or receptive pathologies provoked by a known medical problem or unknown etiology. Notwithstanding limited agreement on how best to define and classify them, speech and language pathologies are not similar; the speech concerns impaired articulation, voice, or fluency. Meanwhile, language dysfunctions affect comprehension, and language production involving semantics, morphology, pragmatics, and syntax in any combination (9,11).

Aphasia after stroke (AAS) is a deterioration or impairment of language processing effected by an acquired cerebral lesion. Bernhardt and colleagues recently published an agreement on AAS common framework recovery definitions where acute ASS recovery/treatments commence within one week of stroke onset, followed by a sub-acute phase in the next 24 weeks, and subsequently chronic phase beyond six months (12-14).

AAS is one of the most devastating symptoms among stroke survivors and severely affects patients' social interactions, quality of life (QOL), and communication. AAS causes the worst consequences in chronic and acute phases (15). The pervasiveness of cognitive ramifications happens in about 1/5 of cases, with aphasia contributing up to 38% of cases (16). The brain region that regulates language (the dominant hemisphere), in approximately 98% of incidents, is the left hemisphere (17).

Several factors are critical in predicting aphasia recovery, including lesion location and size, baseline language ability, and the age at onset. Other factors include patients' pre-stroke language abilities, education, and white matter (WM) preservation status. Status of acute phase management and subsequent language rehabilitation predicts recovery as well (18-20).

Considerable advancements have been made in the past decade to develop pathophysiological models at the systemic and molecular level to understand better and treat AAS clinically, yet the limitation persists. Classical conceptual forms of language processing theorized that two major language centers, namely, Broca and Wernicke, area joined by the arcuate fasciculus and that a lesion to those elemental language areas leads to AAS. New language processing paradigms consider multiple subroutes and the two principal pathways within the predominant left hemisphere (21,22).

Supportive evidence for the new model emerges from functional magnetic resonance imaging-MRI (fMRI), computational modeling, and lesion-symptom mapping. The dual-stream model (DSM) of language processing comprises the dorsal language pathway (DLP), ventral language pathway (VLP), and the interplay of the two pathways. The DLP is involved in phonological processing (speech production and repetition). The mechanism operates by connecting the auditory

cortex in the superior temporal lobe (TL) to the supramarginal gyrus. Then to the premotor cortex and posterior inferior frontal gyrus (FG). Comparatively, VLP subserves semantic processing by correlating the auditory cortex to the ventral anterior TL semantic hub and anterior inferior FG. The VLP and DLP pathways communicate with other regions engaged by involving the posterior-anterior cingulate cortex and ventral insula. In the bilateral hemispheres, the medial superior frontal cortex, intra-parietal sulcus, and dorsolateral prefrontal cortex are involved. Recently, studies demonstrated the importance of specific WM pathways' residual integrity beyond regional gray matter damage. Damage to different parts of the model generates a variety of aphasia subtypes. Hence, a novel approach to AAS focuses on understanding language processing in distributed networks rather than language centers (22-24).

Moreover, there is a developed focus on understanding the molecular pathophysiology of ischemic brain lesion as a dynamic process beyond the direct destruction of network centers and their connections. A cerebral stroke interrupts the cerebral blood flow and consequently harming the brain tissues in altered areas. There are two principal mechanisms suggested in the pathophysiology of cerebral stroke. The first mechanism involves oxidative stress, whereby an impairment to the stability of antioxidant generation with reactive oxygen species (ROS) and other free radicals/oxidants plays a significant pathophysiological role. The second mechanism incorporates the inflammation whereby inflammatory mediators (chemokines/cytokines) and numerous inflammatory cells (monocyte, neutrophils, natural killer cells, and T-cells) into the ischemic brain areas induct neuronal injuries and cell death mechanisms. The stroke-induced lesion results in interhemispheric inhibition disruption, releasing activity in regions homolog to the lesioned area. Repetition impairments induced by acute lesions of the dorsal circuit or the posterior temporoparietal region. More marked in the periventricular WM and arcuate fasciculus. In contrast, more ventral-anterior lesions in the temporal-prefrontal region, specifically between the insular cortex and the putamen in the VLP projection, are associated with comprehension deficits (22,25).

Accurate aphasia diagnosis is vital in stroke care; hence, AAS's proper neuro diagnosis is a crucial management element. Bad clinical experience or expertise may point to conceivably missed or incorrect diagnosis and jeopardized post-stroke care. A thorough evaluation of language skills with relevant instruments in different post-stroke stages is needed to observe language recovery and control speech therapeutics over time. Further, several language examinations are available and incorporate healthcare institutions' tests, informal assessments, and commercial tests. Nevertheless, a diagnostically validated post-stroke aphasia test is needed (18,26).

Owing to the high number mimics hindering accurate AAS diagnosis and dilemmas that face language assessment/test tools, we intended to evaluate the AAS diagnosis formation based on the novel literature. Hence, we explored MEDLINE, Google Scholar, and ScienceDirect for English studies (January 2016 through 2020), spanning from the history-taking skills, neuropsychological assessment, and imaging modalities to tackle the diagnostic dilemmas.

2. The Neurological History Taking in Aphasics

In establishing AAS's diagnosis, the clinician should initially probe the sufferer's natural language, as patterns of language impairment in multilingual speakers with AAS exhibit diversity, with cases, manifest with either parallel or differential language deficits. Studies established the likelihood of polyglots to recover faster in their natural language than in an afterwards learned. In one of the most recent meta-analytic reviews, Kuzmina and colleagues established better performance in the first-acquired language than later-learned languages among polyglots. The difference was determined by whether later-learned languages

were absorbed before seven years of age or later. Cases who received the second language before seven years of age conferred equivalent performance in their languages (27-29).

fMRI based theories point out that polyglots handle-less neural support for language processing. Further anatomical confirmation highlights the caudate nuclei as essential nodes in polyglot language control processes (30). Additional testimony from volumetric interpretations unveiled a significant relationship between multilingual background and right caudate volume. Similarly, vertex-wise studies published a significant expansion of dorsal and anterior parts of the left caudate nucleus (31).

Aphasia manifests with a notably extensive spectrum of signs and forms of encounter, thus mimicking diverse pathologies. To authenticate AAS's diagnosis, the clinicians need to ascertain these three essential questions during history taking 1) Is the presenting complaint exact aphasia? 2) Is the presenting aphasia secondary to stroke? 3) If yes, where is the lesion?

2.1. Is presenting complaint Aphasia?

Both AAS and Dysarthria influence communication skills and social cooperation, generate stigmatization and a stressful caregiver responsibility. Post-stroke patients often experience a co-occurrence of dysarthria and aphasia. Hence, highlighting the need to consider both conditions when conducting patient evaluations. On clinical grounds, when probing speech and language pathologies, the initial aspiration should be to disentangle aphasia from dysarthria, which hallmarks as motor speech dysfunction in which articulation is debilitated in consonants, often with a lazy pace, leading to slurred speech (9,32,33).

Furthermore, notwithstanding muteness being a sign of critical aphasia, it is mandatory to diagnose the mute victim. Muteness can be a neurological manifestation of several pathologies, including frontal lobe pathologies (akinetic mutism) and dysarthria. Similarly, there are autoimmune encephalitis, prion diseases, severe extrapyramidal pathology, and psychosis (catatonia) manifestations. Notably, the ability to write and type with intact language content precludes aphasia in these cases, yet the appearance of unilateral hemiparesis can assist the diagnosis. Notably, a multidisciplinary approach involving the neurologist, immunologist, and psychiatry expert is vital in this type of cases (12,34-37)

However, a nonfluent transitory pathology in which the sufferer presents with initial mutism and then speaks with grammar alteration and pauses (aphemia) lies in a continuum of articulatory and language disorders, warrants differentiation from aphasia. Aphemia is not a genuine language dysfunction, somewhat bearing equivalence to apraxia of speech (AOS). Precisely, AOS involves impaired planning of the motor articulation and speech coordination. Clinically, the production of false speech sounds and sequences of speaker's non-native language sounds, and oddly placed pauses in the speech stream is usually observed (38,39). Recently, a case report of aphemia due to tuberculosis encephalitis (TBE) caused a lesion in the left precentral gyrus in a young girl reported. Clinically, preserved, reading, verbal comprehension, and writing differentiated TBE from AAS while 18F-FDG PET/CT plays a critical role in diagnosis confirmation (40).

2.2. Is the presenting aphasia induced by stroke?

Sudden onset of language complexity proposes a cerebrovascular lesion, frequently accompanied by hemiparesis. Nevertheless, diagnostic dilemmas prevail because several non-vascular complications mimic AAS, further interviewing relatives and extra witnesses obligatory, especially when the aphasia bounds a thorough history taking (41). Generally, a quick resumption of the stroke diagnosis is mandatory to progress with whether the victim is a candidate for acute treatment (42).

Intracerebral hemorrhage (ICH) is a fundamental cause of aphasia, most commonly the basal ganglia hemorrhages associated with hypertension. Unlike ischemic strokes, which exhibit the sudden or stepwise onset, ICH deficits gradually worsen. With headache, vomiting, and obtundation, it is often with better aphasia recovery since ICH compresses cerebral tissue without necessarily destroying it. Putamen hemorrhage is responsible for approximately 85% of aphasia cases admitted in the rehabilitation setting. Maeshima and colleagues established that hematoma type and volume impact aphasia's development following putaminal hemorrhage and significantly determine the patient's fluency and repetition ability. Here, spoken words repetition and Brocas aphasia (BA) are likely to be affected when the hematoma volume is > 20 mL and >40 mL, respectively. Furthermore, there are BA sudden onset cases secondary to hemorrhage from an intracranial tumor (38,43,44). Similarly, postoperative AVM complications reported presenting with acute onset aphasia (45,46).

The diagnosis of neurosyphilis prevails challenging, especially in HIV co-infection, as there are no gold standard tests; hence excellent suspicion is needed. Syphilis meningitis (SM) regularly presents acutely or subacutely in the negation of fever and poses the diagnostic hurdle on establishing aphasia's cause. Notably, a history of cephalalgia vomiting, confusion, nausea, or neck stiffness for up to 48 days should rule out AAS. Consequently, the diagnosis relies on a combination of clinical and CSF findings (47-50). Neuroinvasion occurs in up to 40% of patients. Neurosyphilis is an all-inclusive term utilized to describe *T. pallidum*'s direct intrusion into the nervous system and alter the brain, spinal cord, and peripheral nerves. Meningeal involvement points to complications such as cranial nerve palsies. Vascular syphilis attacks the arterial supply of the brain or spinal cord, rendering ischaemic stroke. Depending on the arterial territory concerned, the small and medium intracranial vessels' endarteritis plays an essential part in the mechanism. The resulting swelling with fibroblasts and collagen propagation in the vessel walls points to intra-luminal narrowing, thrombosis, and ischaemic infarction. A stroke in MCA territory distribution is the most typical exhibition followed by the basilar artery's involvement. Parenchymal neurosyphilis is neurodegenerative (psychosis, memory, emotional lability) (51-53).

Nevertheless, herpes simplex encephalitis (HSE) initial stages may remarkably resemble stroke presentation **Figure 1**. Clinically, it presents with a quick onset of aphasia, hemiplegia, and visual field loss without a history of pyrexia or altered mental status. Barring CSF pleocytosis and brain MRI favors HSE's diagnosis rather than AAS (47,54).

Cerebral venous thrombosis may similarly occur acutely in 44% of the cases with aphasia as a presenting symptom in up to 24% of the patients, especially in left lateral sinus thrombosis (55).

On the other side, the associated sub-acute onset of the classic triad of pyrexia, cephalalgia, which builds progressively over several weeks with co-occurring clouded sensorium or the history seizure, helps to preclude AAS from brain abscess. Further, it is mandatory to explore the history of previous dental implants (56-58). Rarely subcortical aphasia (SCA) reported in deep-seated (thalamic/basal ganglia) abscesses, yet it carries high morbidity and mortality. SCA commonly accompanies hemiparesis; hence rapid CT and MRI are warranted for early drainage and eradicating its primary focus. The most common reported organisms isolated from SCA abscesses are streptococci (*Streptococcus anginosus)* and anaerobes. The capacity for abscess production by S. anginosus is due to leukocidin-like action and thrombin-like venture. Phagocytosis resistance effects brain abscesses by adjacent expanse from a juxta-cranial contaminated site. Hematogenous expanse from a distant site plays the same purpose. Reduced cortical neuronal activity secondary to suppressing input from thalamocortical projections (cortical diaschisis) influences the cortical disturbance witnessed in these cases (59).

Early exclusion of Hashimoto's encephalopathy (HE) from ASS offers early steroids therapy initiation to the HE victims. Based on the presenting history of subacute onset of aphasia associated with tremors, confusion, and automatic muscle jerks, the confirmation with elevated serum anti-thyroid antibodies should help physicians excluding HE (60-62).

Meningioma is the most frequent primary central nervous system (CNS) tumor. The gradual onset of aphasia in the left hemispheric tumors due to edema and mass effect may pose the challenging distinction of tumors from AAS. A left frontal meningioma may provoke a frontal lobe syndrome. Hence, gradually leading to BA and corticospinal pathways quandary. Further, aphasia's sudden onset may arise a few days postoperatively due to the frontal lobe's compression by an enlargement of the postoperative tumor cavity (38,63,64). Extrahepatic metastases occur in approximately 15% of hepatocellular carcinoma (HCC) cases. Nevertheless, metastasis in the CNS is extremely rare, with an incidence of approximately 1.7%. HCC first invades portal and hepatic veins. Afterwards, hematogenous spread tends to occur in the lungs, bones, and adrenal glands. The survival rates of HCC have been increasing, and the CNS could be considered the next metastatic site of HCC (65).

The clinical complex of focal neurodegenerative syndromes, primarily striking language, primary progressive aphasia (PPA), is a crucial AAS mimic. Physicians should probe for family history to rule out AAS. Clinically, AAS can be distinguished based on the gradual (progressive) nature of language deficit, primarily cognitive. Furthermore, evidence of a specific neurodegeneration disorder or the presence of a known pathogenic mutation is diagnostic. Based on specific cognitive and neuroimaging features, the classification of PPA involves three different variants, namely, nonfluent/agrammatic variant (nfvPPA), semantic variant (svPPA), and logopenic variants (lvPPA) (38,63,66-69). svPPA is a fluent form of PPA that intervenes in lexical retrieval that is anatomically pathology centered in anterior and left ventral TL. Comparatively, Wernicke aphasia is a fluent form of AAS, affecting comprehension/ word content expression due to lesions posterior perisylvian regions of the dominant hemisphere. On the contrary, nfvPPA and BA secondary to AAS tend to have more disease locus overlap, with less peculiar syndromic features. Importantly, nfvPPA commonly presents with AOS compared to BA. However, lvPPA pathology is centered on inferior parietal and dorsal TL, manifesting with phonology impairment (39).

Enquiring for past medical history is obligatory in authenticating the diagnosis of AAS in HIV infection cases exhibiting cephalalgia as a first symptom associated with aphasia, hemiparesis, or convulsions. Hence, affirmative CSF studies, MRI, and CT imaging is compulsory (70). Likewise, there are published cases of post malaria neurological syndrome presenting with aphasia, hemiparesis, cortical impairment, tremors, and single cranial nerves palsies (62,71).

An aphasic patient with an altered personality decreased responsiveness, nystagmus, and epilepsy history who exhibits confusion without convulsions, the nonconvulsive status epilepticus (NCSE) should be considered rather than AAS. Nevertheless, responding to anticonvulsants clinically or by an electroencephalogram is NCSE confirmatory (72).

Precluding the past surgical history is not arbitrary when ascertaining the diagnosis of AAS, as lesionectomy, which is thriving in lessening the higher number of seizures in up to 85% of cases, yet carries a risk of complexities, usually 30 days postoperatively, with 2% of cases ending up with AAS (62,73).

Mitochondrial encephalopathy lactic acidosis and stroke (MELAS) are episodic events mimicking ischemic stroke. Clinicians must exclude MELAS in cases presenting with serial seizures succeeded by hemiparesis, psychiatric symptoms, and aphasia. MELAS regularly tend to traverse the known boundaries of vascular territories and variability in MRI apparent diffusion

coefficient. Commonly MELAS involves asymmetrically the temporoparietal-occipital lobes not conforming to the distribution of major arteries. Muscle biopsy for observation of Microscopic changes (ragged-red fibers) and observation of increased serum and cerebrospinal fluid (CSF) lactate level is an essential diagnostic procedure. Further m.3243A > G mutation usually develops in the cerebral cortex, so performing genomic analysis is mandatory (32, 74-76).

The basic pathophysiology of stroke-like episodes remains mostly unknown—proposed mechanisms concern metabolic and vascular systems. Mitochondrial microangiopathy and neuronal vulnerability to heightened energy requirements play an imperative role in the pathogenesis. Additionally, alterations in nitric oxide homeostasis and over-reduction/oxidative stress are another recommended mechanism. L-arginine and L-citrulline's clinical effects to prevent subsequent strokes stress the significance of nitric oxide in MELAS's pathobiology. Likewise, there is an established mechanism linking m.3243A < G mutation in the MELAS pathogenesis. Furthermore, studies report increased DWI/FLAIR signals in the brain MRI among the MELAS's case (75-78).

Furthermore, a clinician should rule out the correlated aura's history as one-sided altered sensation or aphasia since vascular headaches are among the most common disorders treated by neurologists bearing a diagnosis of ophthalmoplegic migraine (79,80). Additionally, when the middle-aged Caucasian men present with neurocognitive signs associated with diarrhea, weight decline, and arthritis, Whipple disease evaluation is necessitated. Testing for periodic acid–Schiff test from small intestine biopsy samples and confirmation of CNS involvement by *Tropheryma whippelei positive CSF* polymerase chain reaction is needed to preclude AAS (62).

Traumatic brain injury as a common cause of aphasia warrants differentiation from AAS; importantly, physicians should rule out the correlated history of altered consciousness, encephalopathy, partial or total loss of memory, and other neurological deficits (79,81).

Obtaining a family social history **Table 1** of alcoholism and poor nutrition can help outline aphasia's etiology. Marchiafava-Bignami disease, known for displaying with psychosis, dementing syndrome, convulsions, hemiplegia, or even sudden onset of coma, can also present with aphasia (56).

Even though clinicians need to prioritized Trichinosis diagnosis when attending a native aphasics from endemic areas (such as the Canadian Arctic/Alaska). Trichinosis should be suspected in aphasia presenting cases with elevated eosinophil count and MRI lesions with border zone distribution, even with a lack of a clear history of consumption of poorly cooked meat. Hypothesized mechanisms link obstruction of vessels by cellular inflammation, toxic effects induced by larvae, and immune allergic vasculitis, hence thrombosis and border zone infarcts. Further, a positive result for trichinosis enzyme-linked immunosorbent assay (ELISA) is confirmed (82,83).

Nevertheless, the family history of cat contact is useful for the distinction of Cat-scratch disease from AAS. The history of cat contact is positive in 90% of the cases. Meanwhile, the preceding scratch or lacerations constitutes 60% of the patient. Symptomatically displaying pyrexia, localized erythematous papule, seizures, and aphasia (62,84).

2.3. Where is the lesion?

Primary language area lesions lead to the incapability to communicate efficiently in terms of expressed, written, or symbolic language; further, the aphasia types depend on the particular cortical damaged area (21). Generally, the left-hemispheric lesion in the anterior circulation points to aphasia, right leg and arm weakness, visual field deficit, decreased right conjugate gaze, troubling writing, reading, and performing calculations (85).

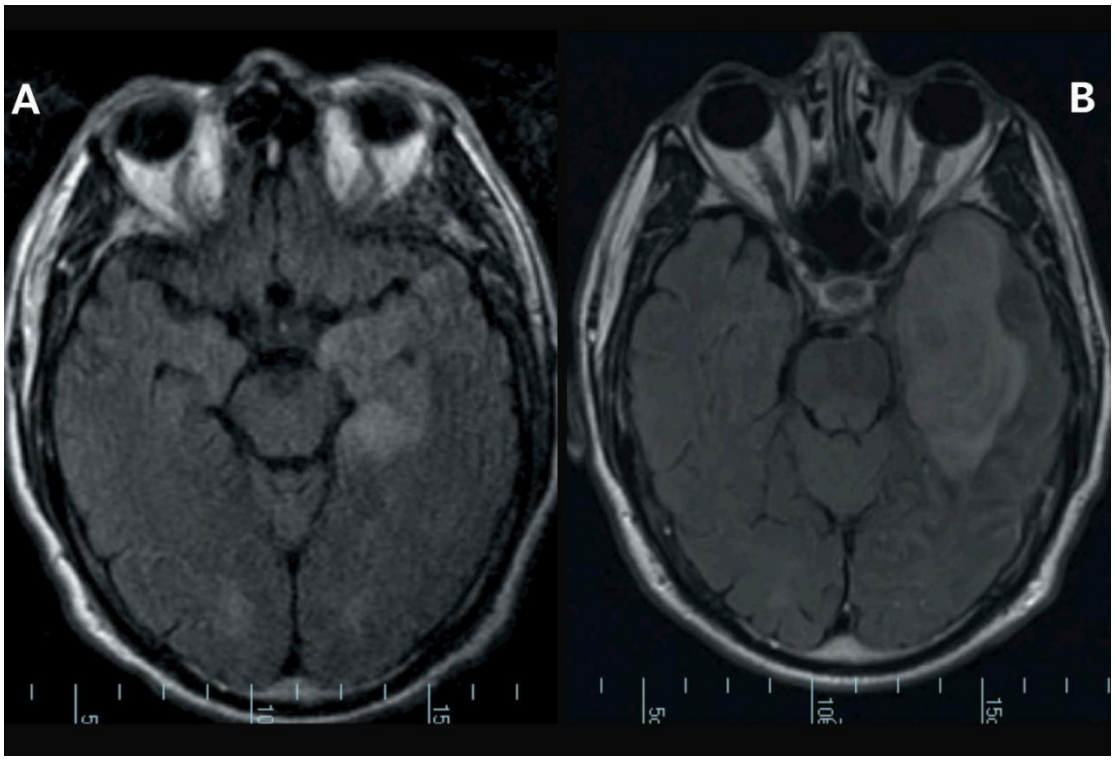

Figure 1 (A) Cerebral MRI of a 72-year-old man, performed first-day post- thrombolysis. He presented with rapid onset aphasia with no associated pyrexia, misdiagnosed for stroke, and underwent thrombolysis. An enhanced FLAIR and increased T2 signal intensity in the medial left TL with slight effacement of the cysts sulci, intimating HSE recorded. **(B)** MRI of the same case fourth-day post-admission when he exhibited pyrexia, shows enhancing parenchymal edema in the TL with sparse mass impression to the adjoining areas observed (54).

Table 1. Overcoming Aphasia After Stroke mimics based on Presenting Patient's History.

Inquire	AAS Mimic	Reference
Onset	SM, HSE,CVT, Brain Abscess, HE	(60-62)
Progression	LFM, PPA	(38,39,63-69)
Associated symptoms	MELAS, OM, WD, TBI	(32,62,74-81)
Past Medical	PMNS, NCSE	(62,71,72)
Past surgical	Lesionectomy	(62,73)
Residency area	Trichinosis	(82)
Family, social	MBD, CSD	(56,62,84).

ABBREVIATION: **AAS**- Aphasia After Stroke, **SM**- Syphilitic Meningitis, **HSE**-Herpes Simplex Encephalitis, **CVT**- Cerebral Venous Thrombosis, **HE**-Hashimoto's Encephalopathy, **LFM**- Left Frontal Meningioma, **PPA**- Primary Progressive Aphasia**, MELAS**-Mitochondrial Encephalopathy Lactic Acidosis and Stroke, **OM**-Ophthalmoplegic Migraine, **WD**-Whipple's Disease, **TBI**-Traumatic Brain Injury, **PMNS**-Post Malaria Neurological Syndrome, **NCSE**-Nonconvulsive Status Epilepticus**, MBD**-Marchiafava-Bignami Disease, **CSD**-Cat-Scratch Disease

Localization of language pathologies to rehabilitate aphasic cases has been a milestone facing several dilemmas to reveal the responsible neural networks. Based on principally observational evaluation and post-mortem in the 19th century, neuroscientists offered the brain/language fundamental knowledge of the 20th century (Geschwind-Wernicke model-GWM), addressed as a classical model (in the introduction section of this article). However, the GWM does not adequately describe the syndromic language neural networks caused by lesions outside the classical regions. Hence the DSM was proposed. The VLP display bilateral organization for language comprehension. Comparatively, the DLP is known for sound-to-motor mapping. Furthermore, even though the cerebellum has not been mentioned in the classical or DSM most recently, the cerebellum role in language production have been proposed and targeted with noninvasive brain stimulation techniques, hence promising future updates on multiple stream model (20,86,87).

Classic aphasic syndromes correlated with particular vascular territories. Many AAS syndromes correlate with altered non-language roles that rely on brain tissue supplied by the corresponding arterial branch. BA accompanies spastic or weak right arm due to the upper portion of the left middle cerebral artery (MCA) lesion. Concerning DSM, Tippett and colleagues insisted on the concept of vascular aphasia by superimposing a map of the vascular territories onto this neuroanatomical model of speech processing to verify that DLP has a supply by the superior branch of the left MCA. Therefore, individuals with BA vascular syndrome typically have (the articulation network/sensorimotor) interface attributed to the DLP disruption. Comparatively, In Wernicke's aphasia, the VLP is mainly supplied by the left MCA's inferior division. Hence, the lesion presents with the lexical interface and destruction of the network to map for sound into meaning (88-92).

During history taking in **Figure 2**, clinicians should observe speech fluency, as nonfluent aphasia symbolizes the frontal language areas anterior to the Rolandic fissure damage. It often presents with slow, nonfluent, pausing telegraphic speech with intact semantic content, implying occlusion of MCA's anterior portion. Comprehension impairment (fluent but vague speech loaded with incorrect words) frequently betokens the temporoparietal lesion posterior to the Rolandic fissure, owing to inferior dominant hemisphere MCA occlusion. Nevertheless, confined undermined repetition may symbolize conduction aphasia. Further, in cases demonstrating the repetition deficit, damage in the Sylvian parietal, temporal area, reflecting DLP disruption must be thought (12,39,88,93).

The abrupt onset of Wernicke's aphasia regularly symbolizes an embolic inferior MCA phenomenon. Simultaneously, basal MCA embolus can lead to global aphasia, internal carotid artery thrombosis, or basal ganglia hemorrhagic stroke. Transcortical motor aphasia is distinct for the anterior cerebral territory, and pure alexia without agraphia is specific to the posterior cerebral artery (PCA) territory (32,38). Even though Transcortical sensory aphasia (TCSA) customarily assigned to parietal or temporal lesions. Lately, Kim and colleagues published cases with left frontal lobe lesions exhibiting TCSA, implying functional interruption amid language hubs in severe stroke (94).

Seizure associated aphasia (SAA) has raised lateralizing significance, guiding seizure origin in the left cerebral region. SAA occurrence is associated with either left-hemispheric seizures or growing seizures from the right to the left hemisphere. The high prevalence reported in patients with parietal-occipital epilepsy. Furthermore, most commonly, frontal and temporal epilepsies are associated with aphasia due to the speech areas (in the dominant frontal and temporal lobe). Conserved responsiveness during or following seizures is a requirement for aphasia identification (95).

Clinically, the evaluation of language function in the initial ictal state can favorably present

valuable data on convulsion localization within TL. Impaired comprehension points to posterior lateral involvement, while anomia and jargon-aphasia associated anterior mediobasal and basal TL lesions (96).

Among pediatric cases with previously normal development, the new onset of Wernicke's aphasia preceding the BA exhibiting difficulties in the processing or interpreting verbal/non-verbal sounds, associated with seizures (absence or tonic-clonic) with marked frequency during sleep, and behavioral abnormalities is supportive of Landau-Kleffner syndrome rather than AAS. Electroencephalogram (EEG) alterations around the temporoparietal area findings of mutations in the GRIN2A gene is confirmatory. In these cases, the theory behind language impairment is aberrations developing during a phase of neural development associated with effective cortical synaptogenesis and functional networks (97,98).

Paramedian infarctions of the thalamus offer a classic triad of a sudden arousal drop, aphasia, and impaired vertical gaze. At the same time, victims with massive left thalamic hemorrhagic stroke may present with speech paucity, verbal paraphasia, and weak voice. Furthermore, severe dysgraphia can present in these cases. Thalamic aphasia localizes left thalamic lesions. In patients presenting with additional anosognosia or spatial neglect, suspicion of bilateral infarction is mandatory. In these cases, aphasia induced mechanism by damage to the ventrolateral nucleus (VLN) and the pulvinar nucleus on the left thalamus theorized. Furthermore, the posterior parietal and TL and thalamic nuclei's disconnection play a significant role in the pulvinar nucleus lesion (17,70,99).

3. The Neuropsychological Assessment

The language dominant hemispheric lesion unevenly disturbs the cognition mechanisms and sensorimotor capabilities. Furthermore, the general language contour represents the peripheral language processing capabilities, the state of central language elements, syntactic skills, and cognition mechanisms that enhance attention (100).

In AAS cases, language evaluation is compulsory for both assisting clinicians in diagnosing the nature and severity of language dysfunction and leading communication therapists in administering rehabilitation. The follow-up is obliged to observe AAS evolving, propose modifications in rehabilitation plans, and estimate the advancement. Published guidelines concerning precise follow-up time are lacking, based on clinical expertise re-evaluation six months following stroke to apprehend substantial gains recommended (18). Furthermore, several proposed screening tools for aphasia in stroke exist, but many tests lack proper verification (101). Hence, the purpose of the neuropsychological assessment is to unveil cognitive shortfalls and processing perplexities that signify the presence of a cerebral lesion focally (80).

Bedside valuation of AAS lets in at least four elementary tests (i) naming abilities, (ii) speech articulateness, (iii) auditory comprehension, and (iv) words repetition; as a rule, language assessment should be performed prior cognitive assessment (102).

More formal testing of language function performed with one of the standardized instruments including the PICA: Porch index of communication ability, WAB: western aphasia battery, AAT: Aachen aphasia test, and the BDAE: Boston diagnostic aphasia examination. Usually, the performance of these tools is by a speech and language therapist. Additionally, the FAST: Frenchay aphasia screening test constructed for regular clinical application by nonprofessional has proved to be valid and reliable (9).

A comprehensive critical neurologic examination assisting neuroanatomic localization accompanied by the mental status examination should be offered (12). Unlike mini-mental state examination(MMSE) and the Montreal cognitive assessment designed for the dementia cases, a recent study comprising 325 post-stroke cases have

confirmed that the Oxford cognitive screen (OCS) a (ten task tool incorporating five cognitive regions) to be a relevant, fine-tuned screening tool for cognitive deficits following stroke (103). Similarly, OCS is a practical tool for identifying and recording significant domain-specific cognitive quandaries in AAS victims compared to the Montreal cognitive assessment (MoCA) (104).

Troubled naming is relatively uniform in all the aphasia syndromes. Usually, during an assessment, the examiner may point to an object and ask patients to name (confrontation naming) or ask the patient to make a list of objects in a division (Word-list generation). Nevertheless, naming tasks are sensitive, but not a specific examination mode regarding aphasia's existence or nonexistence (12). The contemporary study involving 91 patients with AAS (BA subtype) demonstrated that naming and oral reading for language in aphasia 6-Point scale (NORLA-6) to be a potent and credible metric to quantify and identify both naming abilities and to perform a verbal reading in AAS as well as in publishing and clinical perspectives (105).

Comprehension is reviewed by evaluating the patient's comprehension capability, questioning to show particular things, or requesting verbal comments of particular words (106). Despite extended neuropsychological comprehension tools, the new verb semantic comprehension battery is more reliable in identifying semantic shortfalls (107). Basirat and colleagues identified the likelihood of speech segmentation disorder existence among AAS cases, hence registering the importance of evaluating and training speech segmentation when examining AAS patients (108).

In one monolingual pilot research, a brief neuropsychological assessment battery NEUPSILIN for victims with BA, evidence that the short version bears prudence established. Further, NEUPSILIN-Af can assess shortfalls' signs but not the victims' diagnostic outline when evaluating cognitive tasks (109).

Similarly, the aphasia rapid rest (ART) bear usage in language examination in acute post-stroke patients. ART is a twenty-six point scale initially generated and verified in the French language accommodated cross-culturally. Recently, ART validation has been confirmed in the Italian and Portuguese language as well. Despite its simplicity, rapidity, and reproducibility in monitoring initial changes in the acute post-stroke phase, the impossibility of discriminating between aphasic, AOS, and dysarthric pathology is a significant drawback (110).

The current evidence-based guideline on the outcome determination for adults with AAS offered by research outcome measurement in aphasia (ROMA), identified five essential outcome constructs and set consensus for outcome analysis tools. The consensus identified WAB revised (WAB-R) as a standard tool for language outcome measurement and general health questionnaire (GHQ)-12 outcome for emotional well-being assessment. Similarly, ROMA advocated stroke and aphasia QOL Scale (SAQOL-39) for QOL outcomes. Furthermore, no consensus exists for communication measures due to the presence of multiple measures (111). On the contrary, Hilari and colleagues, one year prior, proved that the Scenario Test UK (culturally accommodated version). Initially, from the Dutch language, which evaluates linguistic abilities in an interactive setting with a supportive conversation companion, it is an assuring novel tool for evaluating functional, regular communication for AAS cases (112).

Even though BDAE, Comprehensive aphasia test (CAT), and WAB are the most fully verified linguistic evaluation tools. Nevertheless, they bear a significant drawback of the long duration of administration. Thus, the most contemporary study involving 16 chronic AAS cases confirmed a quick aphasia battery (QAB) is a time-saving tool delivered in approximately 20 minutes (113).

Brief assessment tools help save time for individuals with severe language deficits who may be frustrated and stressed due to lengthy testing sessions that are not cost-effective for serial evaluation. Abou-Elsaad and colleagues offered a

novel finding on one of the brief assessment tools, the Mansoura arabic screening aphasia test (MASAT). Confirming that MASAT executes the initial clinic interview and identify the variety and severity of Arabic speaking AAS cases (114).

Similarly, a firm basis developed for a new German-language "Sprachsystematisches Aphasiescreening" (SAP), proving its capabilities as an essential complement to current assessment and aphasia treatment. Novel findings confirm that SAPS can offer a rationale for therapeutic focus selection, offer an initial point for therapeutic strategy, and integrate home training into the therapy regimen to closely monitor therapeutic outcomes (115).

Guidelines for assessment of depression in AAS cases have yet to be distinguished, merely the stroke aphasic depression questionnaire-10 (SADQ-10) and aphasia depression rating scale (ADRS) seem to be satisfactory models of depression signs post-stroke (116,117). Likewise, the dynamic visual analog mood scales (D-VAMS) are a potent and promising tool with high validity, internal coherence, and reliability for AAS cases; Yet additional research necessitated for the acute stroke (118).

4. Lab test for the exclusion of the mimics

In the acute setting, the management of AAS and stroke is time-dependent. The up-to-date guideline urges IV alteplase (IVA) earlier within a therapeutic window leads to bigger proportional benefits. Hence Noncontrast computed tomography (NCCT), to exclude ICH is recommended as the diagnosis of ischemic stroke can be made accurately based on the clinical presentation and either a negative NCCT or one showing early ischemic changes. Furthermore, Stroke guidelines recommend that among laboratory tests, only the blood glucose testing must be done before the start of IVA in all cases in the absence of coagulopathy suspicion. Hypoglycemia (< 60 mg/dL) and hyperglycemia (>250 mg/dL for Diabetic Ketoacidosis and >600 mg/dL for Hyperosmolar Nonketotic State), can both present with focal neurologic signs and masquerade as stroke. Hypoglycemia requires immediate administration of glucose to avoid permanent brain injury. Hypoglycemia is the most likely diagnosis in patients with altered levels of consciousness, confusion, or a seizure. Subjects with recurrent hypoglycemia experience decreased adrenergic response to lowered glucose levels. Furthermore, defective counter-regulation leads to unawareness of hypoglycemia and hypoglycemia-associated autonomic failure (47,72,119-121).

AAS can be precluded from HSE by laboratory testing. However, controversy still exists. In one case report of a 45 year lady who developed aphasia, CSF examination was decisive, whereby lymphocytic pleocytosis and high protein levels were recognized. Similarly, Polymerase chain reaction measurement for HSE registered a positive outcome in the lumbar puncture (122). On the contrary, Tsuboguchi et al. reported another case of HSE in a woman in the seventies, which displayed a sudden attack of right hemiplegia with an acute stroke diagnosis. The patient then manifested aphasia and high-grade pyrexia but with atypical MRI conclusions and negative CSF pleocytosis (123). Importantly, CSF pleocytosis and head MRI with enhanced intensity on T2 signal and FLAIR support the diagnosis of HSE, preferably than AAS (47,48).

Stroke differentials may estimate for up to 1/3 of all acute stroke consultations. Nevertheless, in the emergency framework, conclusive diagnosis is not regularly achievable. In 2016, Rico and colleagues, published a cased -based report of a 73 year old lady revealing with acute AAS and right hemiparesis. The laboratory examination later authenticated hypercritical hypomagnesemia. This experience advises that lab values are essential for diagnosis to exclude mimics and restrain undesired IVA administration (124).

Practically, for the clinician to rule out AAS from neurosyphilis **Table 2**, a reactive serum FTA-ABS test (reflecting previous syphilis) required. Reactive CSF VDRL test (indicating neurosyphilis) warranted as well. Positive CSF VDRL test is a

diagnostic of neurosyphilis. CSF VDRL has a high specificity of up to 90% but low sensitivity (50,53,125).

Brain abscess has high mortality; however, a notable proportion of cases with properly managed abscess recover entirely; on laboratory examination, sensitive *Staphylococcus intermedius* tissue culture to ampicillin-sulbactam, *Propionibacterium acnes*, and *Streptococcus anginosus* is obligatory (57,59,126).

Neurotoxicity is the most well-known pattern of lithium toxicity. Renal and cardiovascular effects occurred commonly as well, most commonly precipitate by poly-pharmacy and comorbidities. Furthermore, a persistent blood level above 1.5 mEq/L increases neurotoxicity risk. Nevertheless, there are reports of toxicity of lower serum lithium levels of 0.1- 8 mM/L. The neurotoxicity mechanism is still evolving. Early studies highlighted the effect of demyelination and phosphoinositol cycle inhibition. Similarly, change of osmotic balance and hyperstimulation of brain circuits bore consideration. The most recent possible mechanism links lithium to oxidative neurotoxicity due to hydroxyl radical formation secondary to iron efflux from neurons by restraining the tau cascade (127-129).

Madhusoodanan and colleagues reported a case of a lady with records of schizoaffective disorder who were kept on 12 hourly oral Lithium of 300mg and titrated up to 450 mg orally at bedtime covering eight days. At a lithium level of 1.5 mEq/L, aphasia symptoms observed, yet cerebral CT was unremarkable. Aphasia settled solely in 3 days following Lithium discontinuation and rehydration with intravenous fluids (130).

Cefepime is a broadly used antibiotic; there reports of aphasia manifesting as a sign of its neurotoxicity. Cefepime-induced neurotoxicity is confronting to appreciate in the critically ill due to widely varying symptoms. Other presenting symptoms include decreased awareness, encephalopathy, myoclonus, convulsions, and even coma. The toxicity mechanism is linked to increased concentration-dependent competitive GABA antagonism due to its potentiality to cross the blood-brain barrier. Monitoring cefepime serum, CSF concentrations, and creatinine clearances can help n AAS exclusion in the acute setting. However, up to 26% of the cases encountered neurotoxicity, notwithstanding suitable dosing (131).

Similarly, acyclovir toxicity can mimic aphasia presenting symptoms. Rapid recognition, diagnosis, and treatment of acyclovir toxicity will reduce the chances of permanent neurologic sequela. Efficacious acyclovir levels in the serum at 9 - 18 mg/mL. The exact mechanism for acyclovir-induced neurotoxicity remains unclear. Nevertheless, caution should be focused on old patients (due to decreased muscle mass) and decreased intravascular volume due to decreased renal clearance (132).

Table 2. Laboratory Studies to assist Aphasia After Stroke Mimics exclusion.

Aphasia after Stroke Mimic	Laboratory test	Findings	Reference
Neurosyphilis	Serum FTA-ABS	Reactive	(50,53,125)
	CSF VDRL	Reactive	
HSE	CSF PCR	HSE Positive	(122)
Brain Abscess	Tissue culture	Positive *S. intermedius*/ *P. acnes* / *S. anginosus*	(57,59,126)
PPA	Genetic screening	TDP-43 /tau pathology	(39,47,72)
Hashimoto's encephalopathy	Serum anti-thyroid antibodies	Increased	(60-62)

MELAS	Serum/CSF Lactate	Increased	(32, 74-78)
	Genomic Analysis	m.3243A>G mutation	
Whipple's Disease	PAS	Positive	(62)
	CSF PCR	Positive *T whippelei*	
Trichinosis	ELISA	Positive	(82,83)
	Eosinophil	Increased	
Hypoglycemia	Blood Glucose	Decreased	(47,72,119-121)
Hyperglycemia	Blood Glucose	Increased	(72,119)
Hypomagnesemia	Serum magnesium levels	Decreased	(124)
Drug Toxicity (Lithium/Cefepime/Acyclovir)	(Specific drug) serum levels	Increased	(127-132)

ABBREVIATION: **FTA-ABS**: Fluorescent Treponemal Antibody Absorbed, **CSF**: Cerebrospinal Fluid, **VDRL**: Venereal Disease Research Laboratory, **HSE**: Herpes Simplex Encephalitis, **PCR:** Polymerase Chain Reaction, **PAS**: Periodic Acid–Schiff test, **ELISA**: Enzyme-linked Immunosorbent Assay, **PPA**: Primary Progressive Aphasia, **MELAS**: Mitochondrial Encephalopathy Lactic Acidosis and Stroke

5. Neuroimaging Modalities

New measures of stroke false-negative cases approximate up to 26%. In contrast, false-positive cases estimate for up to 43%. Incompetency in stroke diagnosis can restrain time-sensitive therapies and lead to correlated secondary consequences; diagnosis efficiency requires fast clinical thinking in the acute setting (133).

Acute ischemic stroke (AIS) prevails as a clinical and imaging hurdle, corresponding to up to 30% of emergency cases in the acute setting. Cerebral imaging is the base for accurate diagnosis distinguishing the stroke mimics (134). Further, the use of MRI at baseline contracts the dimension of cases with the mimics (135).

The purpose neuroimaging is to contrast AIS from ICH, as well as to diagnose non-vascular events. Neuroimaging modalities may serve as a functional consequence assessment and prognosticate the effectiveness of rehabilitation in addition to functional evaluation scales (102,136).

A cerebral NCCT can outline the most utmost focal anatomical lesions influencing cerebral linguistic areas. Besides, following new-onset acute ischemic stroke may be expected in the opening 24 hours (12,137). Cerebral MRI is moderately extra appreciable than CT at distinguishing morphologic irregularities and is the more favored. Sagittal, coronal and axial plane imaging enables accurate mapping of lesions in the established neural language domains, especially in the temporal cortex proximate to the petrous bone, and extra impressible in the exposure of tissue pathologies such as initial infarction variations, the anatomical cortical-subcortical aphasia differentiation in acute strokes by diffusion-weighted MRI (137). Field and colleagues described a case-based report of a Caucasian lady who exhibited AAS. Supplementary workup exposed common carotid artery intra-luminal obstruction, with an implication of early presentation of Takayasu arteritis. This observation designates the necessity of imaging to eliminate embolus sources' grounds to delimit mimics (138).

Cerebral imaging is the base for the determination of Brain Abscess to exclude AAS. MRI preferable if promptly accessible, as it

concedes expected benefits above contrast-enhanced CT, including more commendatory resolution, quicker apprehension of injuries, admitting description of new lesions, and lack of toxicity from the contrast agent (57,139).

Cerebral contrast-enhanced CT is obligatory when a cerebral tumor such as frontal meningioma is a concern. However, in one follow-up case, it was proclaimed using an MRI scan to authenticate the frontal meningioma diagnosis invading the Brocas Area (140,141).

An electroencephalogram(EEG) is useful in patients with isolated stereotyped aphasia to preclude the focal epileptic locus's possibilities and confining seizure discharge. The EEG can render proof whether aphasia is an ictal or postictal event and can provide immediate hints to aphasia after tumor lesions or herpes simplex encephalitis (38). Further, electromyography is also applied to diagnose neuromuscular dysfunctions generating dysarthria (142).

Language activation with fMRI or PET has a significant contribution to language study. These methods support mapping cerebral regions that arouse throughout the language functions following strokes and can be used to examine the recovery pattern. Further, additional studies have shown right hemispheric activation in recovering AAS cases. Other modern imaging modalities include task fMRI, Diffusion imaging, and MR spectroscopy (143).

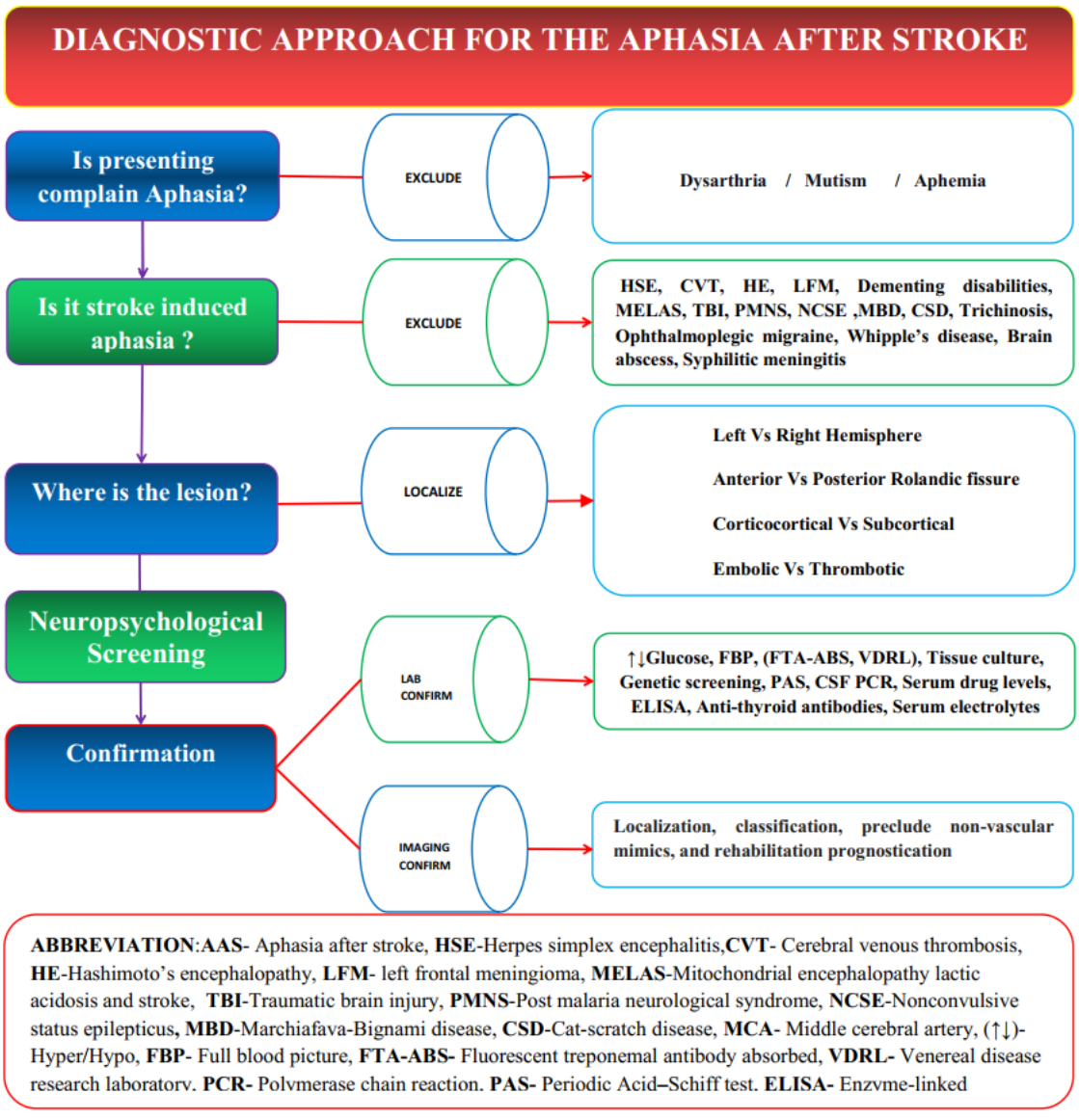

Figure 2. The Neurodiagnostic approaches to overcome diagnostic dilemmas, based on the novel literature.

The first three rows are the triad of inquiries to perform thorough history taking. Neuropsychological screening, laboratory tests, and neuroimaging follow them. Last row comprises a list of abbreviations.

6. Conclusions

AAS is a decline or impairment of language processing effected by acquired cerebral lesions, leading to the worst consequences in chronic and acute phases. Owing to the extensive spectrum of mimicking pathologies posing a hurdle to authenticate AAS's diagnosis, based on the novel literature, we proposed three sets of questions that a physician requires to pay attention during history taking.

During history, clinicians must initially establish whether the patient presenting complaint is actual aphasia by differentiating aphasia from dysarthria, mutism, catatonia, and aphemia. Then demonstrate whether the presenting aphasia is stroke-induced, to preclude aphasia from mimics based on onset of language complexity, the progress of aphasia, associated symptoms, past medical history, history of lesionectomy, and family, social, and residency area. Finally, offer specific questions for localizing the lesions. Here, the goal is to establish whether the location is in the left-hemispheric region, anterior/posterior Rolandic fissure, perisylvian, cortical, or sub-cortical region. Then, determine if AAS is embolic, thrombotic etiology, and predict a specific MCA infarctions portion.

For AAS assessment, QAB appears to be a time-saving tool owing to time-saving (delivered in 20 minutes) compared to the most verified language evaluation tools (BDAE, CAT, and WAB). OCS bears proof as a fine-tuned screening tool for stroke-related cognitive deficits compared to MMSE and MoCA. New guidelines offered consensus regarding the valuable tool in evaluating QOL, language, and emotional well-being, yet controversy regarding suitable means for communication assessment exists. Further, the assessment guidelines for the AAS-depression comorbidity are lacking, but SADQ-10, ADRs, and D-VAMS seem to be potent validated tools. Further, specific laboratory investigations and imaging modalities for AAS mimic exclusion covered in this review, yet neuroimaging remain the cornerstone for the accurate AAS diagnosis, classification, precluding the mimics, and rehabilitation prognostication.

Declarations

1) ***Consent to publication***
   We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2) ***Ethical approval and consent to participants***
   Not applicable.
3) ***Disclosure of conflict of interests***
   No conflict of interest exists.
4) ***Funding***
   None
5) ***Availability of data and material***
   We declare that the data supporting the results reported in the article are available in the published article.
6) ***Authors' Contributions***
   Authors contributed to this paper with the design (SSM), literature search (SSM, YL), drafting (SSM), revision (SSM,YL and XC), editing (SSM,YL and XC) and final approval (SSM,YL and XC).
7) ***Acknowledgement***
   None
8) ***Authors' biography***
   None

References

1. Gowshall M, Taylor-Robinson SD. The increasing prevalence of non-communicable diseases in low-middle income countries: the view from Malawi[J]. Int J Gen Med. 2018;11:255-264.
2. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013-2020.*http://www.who.int/nmh/events/ncd_action_plan/en/* (Date accessed:September 28, 2020)
3. Reddy KS. Measuring mortality from non-communicable diseases: broadening the band[J]. Lancet Glob Health. 2020;8(4):e456-e457.
4. Johnson CO, Nguyen M, Roth GA, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the global burden of disease study 2016[J]. The Lancet Neurology. 2019;18(5):439-458.
5. Ekker MS, Boot EM, Singhal AB, et al. Epidemiology, aetiology, and management of ischaemic stroke in young adults[J]. Lancet Neurol. 2018;17(9):790–801.
6. Bulletin of the World Health Organization 2016;94:634-634A.
7. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, Wang L, Jiang Y, Li Y, Wang Y, Chen Z, Wu S, Zhang Y, Wang D, Wang Y, Feigin VL; NESS-China Investigators. Prevalence, incidence, and mortality of stroke in China: Results from a nationwide population-based survey of 480 687 adults[J]. Circulation. 2017;135(8):759-771.
8. Gao Y, Jiang B, Sun H, Ru X, Sun D, Wang L, Wang L, Jiang Y, Feigin VL, Wang Y, Wang W. The burden of stroke in China: Results from a nationwide population-based epidemiological survey[J]. PLoS One. 2018;13(12):e0208398.
9. Soo Y, Leung H, Wong LK. What are this patient's problems? A problem-based approach to the general management of stroke. Warlow's Stroke: Practical Management[M]. 2019:4202808. (pp. 481-578).
10. Mitchell C, Gittins M, Tyson S, Vail A, Conroy P, Paley L, Bowen A. Prevalence of aphasia and dysarthria among inpatient stroke survivors: describing the population, therapy provision and outcomes on discharge[J]. Aphasiology. 2020 May 4:1-1.
11. Vuolo J, Goffman L. Language skill mediates the relationship between language load and articulatory variability in children with language and speech sound disorders[J]. J Speech Lang Hear Res. 2018 10;61(12):3010-3022.
12. Biller, José. Practical neurology[M].Wolters Kluwer/Lippincott Williams & Wilkins Health, 2017.
13. Bernhardt J, Hayward KS, Kwakkel G, Ward NS, Wolf SL, Borschmann K, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: The stroke recovery and rehabilitation roundtable taskforce[J]. Int J Stroke. 2017;12(5):444–50.
14. Msigwa SS, Cheng X. The management of subacute and chronic vascular aphasia: an updated review[J]. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2020;56(1):1-3.
15. Lazar RM, Boehme AK. Aphasia as a predictor of stroke outcome[J]. Curr Neurol Neurosci Rep. 2017;17(11):83.
16. Rockenbach SP. Post-stroke rehabilitation : identification of speech-language disorders signs and symptoms by physicians and nurses in primary health care[J]. 2019;1782(2):1-7.
17. Gregory, A M, and E H. Duane. Fundamental neuroscience for basic and clinical applications[M]. Fifth edition . Elsevier, 2018.
18. Mattioli F. The clinical management and rehabilitation of post stroke aphasia in Italy: evidence from the literature and clinical experience[J]. Neurol Sci. 2019;40(7):1329-1334.
19. Msigwa SS, Li Y, Cheng X. Treatment and prognosis of aphasia after stroke[J]. Global Journal of Neuroscience. 2019;1(1):19-28.
20. Zhang J, Wei X, Xie S, Zhou Z, Shang D, Ji R, Yu Y, He F, Du Y, Ye X, Luo B. Multifunctional roles of the ventral stream in

language models: Advanced segmental quantification in post-stroke aphasic patients[J]. Front Neurol. 2018; 9:89.
21. Krebs C, Akesson EJ, Weinberg J. Lippincott's Illustrated Reviews: Neuroscience[M]. Wolters Kluwer/Lippincott Williams & Wilkins Health, 2018.
22. Thiel A, Zumbansen A. The pathophysiology of post-stroke aphasia: A network approach[J]. Restor Neurol Neurosci. 2016 Jun 13;34(4):507-18.
23. McKinnon ET, Fridriksson J, Basilakos A, Hickok G, Hillis AE, Spampinato MV, Gleichgerrcht E, Rorden C, Jensen JH, Helpern JA, Bonilha L. Types of naming errors in chronic post-stroke aphasia are dissociated by dual stream axonal loss[J]. Sci Rep. 2018;8(1):14352.
24. Stefaniak JD, Halai AD, Lambon Ralph MA. The neural and neurocomputational bases of recovery from post-stroke aphasia[J]. Nat Rev Neurol. 2020;16(1):43-55.
25. Patnaik R, Tripathi AK, Dwivedi A, editors. Advancement in the pathophysiology of cerebral stroke[M]. Springer Singapore, 2019.
26. Rohde A, Worrall L, Godecke E, O'Halloran R, Farrell A, Massey M. Diagnosis of aphasia in stroke populations: A systematic review of language tests[J]. PLoS One. 2018;13(3):e0194143.
27. Ropper AH, Samuels MA, Klein JP, Prasad S. Adams and victor's principles of neurology[M]. 11th ed. New York: McGraw-Hill, 2019
28. Kuzmina E, Goral M, Norvik M, Weekes BS. What influences language impairment in bilingual aphasia? A meta-analytic review[J]. Frontiers in psychology. 2019;10:445.
29. Mariën P, van Dun K, Van Dormael J, Vandenborre D, Keulen S, Manto M, Verhoeven J, Abutalebi J. Cerebellar induced differential polyglot aphasia: A neurolinguistic and fMRI study[J]. Brain Lang. 2017;175:18-28.
30. Jouravlev O, Mineroff Z, Blank IA, Fedorenko E. The small and efficient language network of polyglots and hyper-polyglots[J]. Cereb Cortex. 2020:bhaa205.
31. Hervais-Adelman A, Egorova N, Golestani N. Beyond bilingualism: multilingual experience correlates with caudate volume. Brain Struct Funct. 2018;223(7):3495-3502.
32. Salardini A, Biller J. The hospital neurology book[M]. McGraw-Hill Education, 2016.
33. Kim G, Min D, Lee EO, Kang EK. Impact of co-occurring dysarthria and aphasia on functional recovery in post-stroke patients[J]. Ann Rehabil Med. 2016;40(6):1010-1017.
34. Tariq M, Afridi MI, Saleem D, Pirzada S. Catatonic schizophrenia: Cases with possible genetic predisposition[J]. Cureus. 2019;11(4):e4525.
35. Zubair UB, Majid H. Anti-NMDA Receptor encephalitis in a young girl with altered behaviour and abnormal movements[J]. J Coll Physicians Surg Pak. 2018;28(8):643-644.
36. Iwasaki Y, Mori K, Ito M, Kawai Y, Hoshino KI, Kawabata Y, Mimuro M, Yoshida M. Gastrostomy in patients with prion disease[J]. Prion. 2017;11(3):186-194.
37. Fu R, Yanfang C, Shaohua C. Case of catatonia misdiagnosed with coma[J]. Gen Psychiatr. 2020;33(1):e100059.
38. Kirshner HS. Aphasia and aphasic syndromes. Neurology in Clinical Practice[M]. 7th ed. Philadelphia, PA: Butterworth Heniemann Elsevier, 2016:128-144
39. Grossman M, Irwin DJ. Primary Progressive Aphasia and Stroke Aphasia[J]. Continuum (Minneap Minn). 2018;24(3, BEHAVIORAL NEUROLOGY AND PSYCHIATRY):745-767.
40. Maramattom BV, Thomas J, Joseph S. Tuberculous encephalitis with aphemia detected only by 18F-Fluorodeoxyglucose-positron emission tomography[J]. Ann Indian Acad Neurol. 2019;22(4):527-529.
41. Tsementzis SA. Differential diagnosis in neurology and neurosurgery[M]. Thieme; 2019.

42. Denny MC, Ramadan AR, Grotta J, Savitz SI. Acute Stroke Care[M]. Cambridge University Press, 2019.
43. Maeshima S, Okamoto S, Okazaki H, Funahashi R, Hiraoka S, Hori H, Yagihashi K, Fuse I, Tanaka S, Asano N, Sonoda S. Aphasia following left putaminal hemorrhage at a rehabilitation hospital[J]. Eur Neurol. 2018;79(1-2):33-37.
44. Seki S, Kamide T, Tamase A, Mori K, Yanagimoto K, Nomura M. Subarachnoid and intracerebral hemorrhage from intracranial hemangiopericytoma: An uncommon cause of intracranial hemorrhage[J]. Neuroradiol J. 2016;29(3):183-6.
45. Cheng CY, Shetty R, Sekhar LN. Microsurgical resection of ruptured large left temporo-occipital arteriovenous malformation: 3-dimensional operative video[J]. Oper Neurosurg (Hagerstown). 2018;15(6):E86.
46. Wakui D, Ito H, Takasuna H, Onodera H, Oshio K, Tanaka Y. Surgical removal of an arteriovenous malformation in the anterior perforated substance in a pregnant woman[J]. Surg Neurol Int. 2018;9:117.
47. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's manual of medicine[M]. McGraw-Hill Education, 2020.
48. Budhram A, Silverman M, Burneo JG. Neurosyphilis mimicking autoimmune encephalitis in a 52-year-old man[J]. CMAJ. 2017;189(29):E962–E965.
49. Perez Barragán E, Urdez Hernández E, Pérez Orozco B, Sánchez González M. Meningovascular neurosyphilis with basilar artery thrombosis in HIV patient[J]. J Infect Public Health. 2018;11(3):439-441.
50. Tuddenham S, Ghanem KG. Neurosyphilis: Knowledge Gaps and Controversies[J]. Sex Transm Dis. 2018;45(3):147-151.
51. Hobbs E, Vera JH, Marks M, Barritt AW, Ridha BH, Lawrence D. Neurosyphilis in patients with HIV[J]. Pract Neurol. 2018;18(3):211-218.
52. Gonzalez H, Koralnik IJ, Marra CM. Neurosyphilis[J]. Semin Neurol. 2019;39(4):448-455.
53. Krishnan D, Zaini SS, Latif KA, Joseph JP. Neurosyphilis presenting as acute ischemic stroke[J]. Clin Med (Lond). 2020;20(1):95-97.
54. Win T, Maham N, Kumar S. Herpes encephalitis : a stroke mimicker[J]. Journal of Community Hospital Internal Medicine Perspectives.
55. Luo Y, Tian X, Wang X. Diagnosis and treatment of cerebral venous thrombosis: A Review[J]. Front Aging Neurosci. 2018;10:2.
56. Brust JC. Current diagnosis & treatment neurology[M]. McGraw Hill Professional, 2018.
57. Odunukan OW, Masannat F, Baka JJ. Propionibacterium acnes brain abscess in an immunocompetent man in the absence of prior neurosurgery[J]. S D Med. 2016;69(2):71-3.
58. Steiner C, Bottini GB, Gaggl A. Brain abscess caused by dental peri-implantitis[J]. Br J Oral Maxillofac Surg. 2020:S0266-4356(20)30300-4.
59. Hernandez Jimenez JM, Vahdat K, Serrano Santiago IA, Morales Hernandez MDM, Isache CL, Sands M. Thalamic bacterial abscess presenting with hemiparesis and expressive aphasia[J]. IDCases. ;13:e00417.
60. Laurent C, Capron J, Quillerou B, et al. Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT): Characteristics, treatment and outcome in 251 cases from the literature[J]. Autoimmun Rev. 2016;15(12):1129–1133.
61. Brown J, Sardar L. An autoimmune cause of confusion in a patient with a background of hypothyroidism [published online ahead of print, 2019 May 23][J]. Endocrinol Diabetes Metab Case Rep. 2019;2019:19-0014.
62. Lisak RP, Truong DD, Carroll WM, Bhidayasiri R, editors. International neurology[M]. John Wiley & Sons, 2016.

63. Kumar, Parveen J. Kumar Et Clark's clinical medicine[M]. Edinburgh: Saunders Elsevier, 2017.
64. Fujimori T, Shindo A, Ogawa D, Okada M, Hatakeyama T, Okauchi M, Kawanishi M, Miyake K, Tamiya T. A rare case of postoperative symptomatic cyst formation after resection of a large convexity meningioma[J]. World Neurosurg. 2019;127:160-164.
65. Sartori Balbinot R, Facco Muscope AL, Dal Castel M, Sartori Balbinot S, Angelo Balbinot R, Soldera J. Intraparenchymal hemorrhage due to brain metastasis of hepatocellular carcinoma[J]. Case Rep Gastroenterol. 2017;11(3):516-525.
66. Meyer MA. Neurologic disease: a modern pathophysiologic approach to diagnosis and treatment[M]. Springer, 2016.
67. Samuels MA, Ropper AH, editors. Samuels's manual of neurologic therapeutics[M]. Lippincott williams & wilkins, 2017
68. Prabhakar AT, Mathew V, Sivadasan A, Aaron S, George A, Alexander M. Clinical profile of primary progressive aphasias in a tertiary care centre from India[J]. Int J Speech Lang Pathol. 2019;21(6):547-552.
69. Tee BL, Gorno-Tempini ML. Primary progressive aphasia: a model for neurodegenerative disease[J]. Curr Opin Neurol. 2019;32(2):255-265.
70. Singh MB, Bhatia R, editors. Emergencies in neurology[M]. Springer, 2019.
71. Tamzali, Y., Demeret, S., Haddad, E. et al. Post-malaria neurological syndrome: four cases, review of the literature and clarification of the nosological framework[J]. Malar J 17, 387 (2018).
72. Roger P., David A. Greenberg, Michael J. Aminoff. Clinical Neurology[M].10th ed. Stamford, Conn: Appleton & Lange, 2018
73. Rolston JD, Englot DJ, Knowlton RC, Chang EF. Rate and complications of adult epilepsy surgery in North America: Analysis of multiple databases[J]. Epilepsy Res. 2016;124:55–62.
74. Montano V, Simoncini C, LoGerfo A, Siciliano G, Mancuso M. Catatonia as prominent feature of stroke-like episode in MELAS[J]. Neurol Sci. 2020.
75. Nukui T, Matsui A, Niimi H, Yamamoto M, Matsuda N, Piao JL, Noguchi K, Kitajima I, Nakatsuji Y. Cerebrospinal fluid ATP as a potential biomarker in patients with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke like episodes (MELAS)[J]. Mitochondrion. 2020;50:145-148.
76. Oyama M, Iizuka T, Nakahara J, Izawa Y. Neuroimaging pattern and pathophysiology of cerebellar stroke-like lesions in MELAS with m. 3243A> G mutation: a case report[J]. BMC neurology. 2020;20:1-6.
77. Almasi M, Motamed MR, Mehrpour M, Haghi-Ashtiani B, Haji Akhondi F, Nilipour Y, Fereshtehnejad SM. A Mitochondrial disorder in a middle age iranian patient: Report of a rare case[J]. Basic Clin Neurosci. 2017 Jul-Aug;8(4):337-341.
78. Wang R, Li Y, Lin J, Sun C, Chen N, Xu W, Hu B, Liu X, Geng D, Yang L. Altered spontaneous brain activity at attack and remission stages in patients with mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS): Beyond stroke-like lesions[J]. Mitochondrion. 2020;54:49-56.
79. Caplan LR, Biller J. Nonatherosclerotic vasculopathies. Caplan’s Stroke. A Clinical Approach[M].2016:385-438 .
80. Mumenthaler M, Mattle H. Fundamentals of neurology: an illustrated guide[M]. Thieme, 2017.
81. Degen RM, Fink ME, Callahan L, Fibel KH, Ramsay J, Kelly BT. Brain contusion with aphasia following an ice hockey injury[J]. Phys Sportsmed. 2016;44(3):324-6.
82. Goldman L, Schafer AI. Goldman's cecil medicine[M]. Elsevier Health Sciences, 2020.

83. Rosca EC, Simu M. Border zone brain lesions due to neurotrichinosis[J]. International Journal of Infectious Diseases. 2018;67:43-5.
84. Canneti B, Cabo-López I, Puy-Núñez A, et al. Neurological presentations of Bartonella henselae infection[J]. Neurol Sci. 2019;40(2):261–268.
85. Caplan LR, Fernando Barinagarrementeria .Diagnosis and the clinical encounter .In: Caplan LR, ed. Caplan's Stroke: A Clinical Approach[M]. 5th ed. Cambridge: Cambridge University Press, 2016:55 -77 .
86. Nasios G, Dardiotis E, Messinis L. From Broca and Wernicke to the neuromodulation era: Insights of brain language networks for neurorehabilitation[J]. Behav Neurol. 2019;2019:9894571.
87. Sebastian R, Saxena S, Tsapkini K, Faria AV, Long C, Wright A, et al.Cerebellar tDCS: a novel approach to augment language treatment poststroke[J]. Front Hum Neurosci. 2017;10:695
88. Tippett DC, Hillis AE. Vascular aphasia syndromes. In: Neurobiology of language[M]. Academic Press, 2016.p. 913-922.
89. Fridriksson J, Yourganov G, Bonilha L, Basilakos A, Den Ouden DB, Rorden C. Revealing the dual streams of speech processing[J]. Proc Natl Acad Sci U S A. 2016;113(52):15108-15113.
90. Tremblay P, Dick AS. Broca and Wernicke are dead, or moving past the classic model of language neurobiology[J]. Brain Lang. 2016;162: 60–71.
91. Sreedharan S, Arun KM, Sylaja PN, Kesavadas C, Sitaram R. Functional connectivity of language regions of stroke patients with expressive aphasia during real-time functional magnetic resonance imaging based neurofeedback[J]. Brain Connect. 2019;9(8):613-626.
92. Grechuta K, Bellaster BR, Munné RE, Bernal TU, Hervás BM, San Segundo R, Verschure PF. The effects of silent visuomotor cueing on word retrieval in broca's aphasies: A pilot study. In2017 International Conference on Rehabilitation Robotics (ICORR) 2017 Jul 17 (pp. 193-199). IEEE.
93. Champney TH. Essential clinical neuroanatomy[M]. John Wiley & Sons, 2016.
94. Kwon M, Shim WH, Kim SJ, Kim JS. Transcortical sensory aphasia after left frontal lobe infarction: Loss of functional connectivity[J]. Eur Neurol. 2017;78(1-2):15–21. doi:10.1159/000477167
95. Loesch AM, Steger H, Losher C, Hartl E, Rémi J, Vollmar C, Noachtar S. Seizure-associated aphasia has good lateralizing but poor localizing significance[J]. Epilepsia. 2017;58(9):1551-1555.
96. Trebuchon A, Lambert I, Guisiano B, McGonigal A, Perot C, Bonini F, Carron R, Liegeois-Chauvel C, Chauvel P, Bartolomei F. The different patterns of seizure-induced aphasia in temporal lobe epilepsies. Epilepsy Behav. 2018;78:256-264.
97. Muzio MR, Cascella M, Al Khalili Y. Landau Kleffner syndrome. 2020 Jul 4. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2020.
98. Katyal R, De Sousa E, Sultan F. A rare case of prolonged ictal aphasia[J]. Neurodiagn J. 2019;59(2):104-111.
99. Moalla KS, Othman M, Massoud LB, Kamoun F, Triki C. Unusual presentation of childhood reversible angiopathy: Aphasia due to acute bilateral paramedian thalamic infarct[J]. Journal of Pediatric Neurology. 2018;16(04):248-52.
100. Beeson PM, Bayley C, Shultz C, Rising K. Maximising recovery from aphasia with central and peripheral agraphia: The benefit of sequential treatments[J]. Neuropsychological Rehabilitation. 2019;29(9):1399-1425.
101. El Hachioui H, Visch-Brink EG, de Lau LM, van de Sandt-Koenderman MW, Nouwens F, Koudstaal PJ, Dippel DW. Screening tests for aphasia in patients with stroke: a systematic review[J]. J Neurol. 2017;264(2):211-220.

102. Brainin M, Heiss WD, editors. Textbook of stroke medicine[M]. Cambridge University Press, 2019.
103. Mancuso M, Demeyere N, Abbruzzese L, et al. Using the Oxford cognitive screen to detect cognitive impairment in stroke patients: A comparison with the mini-mental state examination[J]. Front Neurol. 2018;9:101.
104. Demeyere N, Riddoch MJ, Slavkova ED, et al. Domain-specific versus generalized cognitive screening in acute stroke[J]. J Neurol. 2016;263(2):306-315.
105. Pitts LL, Hurwitz R, Lee JB, Carpenter J, Cherney LR. Validity, reliability and sensitivity of the NORLA-6: Naming and oral reading for language in aphasia 6-point scale[J]. International Journal of Speech-Language Pathology. 2018;20(2):274-283.
106. Mesulam MM . Aphasia, Memory Loss, Hemispatial neglect, frontal Syndromes, and other cerebral disorders ***. In:Harrison's Principles of Internal Medicine***[M]***. 20e New York, NY: McGraw-Hill; 2018.157 -166***
107. Alyahya RSW, Halai AD, Conroy P, Lambon Ralph MA. The behavioural patterns and neural correlates of concrete and abstract verb processing in aphasia: A novel verb semantic battery[J]. NeuroImage: Clinical. 2018;17:811-825.
108. Basirat A, Allart É, Brunellière A, Martin Y. Audiovisual speech segmentation in post-stroke aphasia: a pilot study[J]. Topics in Stroke Rehabilitation. 2019;26(8):588-594.
109. Rodrigues J de C, Machado W de L, da Fontoura DR, et al. What neuropsychological functions best discriminate performance in adults post-stroke?[J]. Applied Neuropsychology: Adult. 2019;26(5):452-464.
110. Panebianco M, Zavanone C, Dupont S, et al. The inter-rater reliability of the Italian version of aphasia rapid test (ART) for acute ischemic stroke[J]. Neurol Sci. 2019;40(10):2171-2174.
111. Wallace SJ, Worrall L, Rose T, et al. A core outcome set for aphasia treatment research: The ROMA consensus statement[J]. International Journal of Stroke. 2019;14(2):180-185.
112. Hilari K, Galante L, Huck A, Pritchard M, Allen L, Dipper L. Cultural adaptation and psychometric testing of the scenario test UK for people with aphasia: Adaptation and testing of the scenario test UK for people with aphasia[J]. International Journal of Language & Communication Disorders. 2018;53(4):748-760.
113. Wilson SM, Eriksson DK, Schneck SM, Lucanie JM. A quick aphasia battery for efficient, reliable, and multidimensional assessment of language function. Jäncke L, ed[J]. PLoS ONE. 2018;13(2):e0192773.
114. Abou-Elsaad T, Baz H, Belal T, Elsherbeny S. Developing an Arabic screening test for adult-onset chronic aphasia[J]. Folia Phoniatr Logop. 2018;70(2):74-81.
115. Krzok F, Rieger V, Niemann K, et al. The novel language-systematic aphasia screening SAPS: screening-based therapy in combination with computerised home training[J]. International Journal of Language & Communication Disorders. 2018;53(2):308-323.
116. Laures-Gore JS, Farina M, Moore E, Russell S. Stress and depression scales in aphasia: relation between the aphasia depression rating scale, stroke aphasia depression questionnaire-10, and the perceived stress scale[J]. Topics in Stroke Rehabilitation. 2017;24(2):114-118.
117. Van Dijk MJ, De Man-Van Ginkel JM, Hafsteinsdóttir TB, Schuurmans MJ. Identifying depression post-stroke in patients with aphasia: A systematic review of the reliability, validity and feasibility of available instruments[J]. Clin Rehabil. 2016;30(8):795-810.
118. Barrows PD, Thomas SA. Assessment of mood in aphasia following stroke: validation of the dynamic visual analogue mood scales (D-VAMS)[J]. Clin Rehabil. 2018;32(1):94-102.

119. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 Update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American heart association/American stroke association[J]. Stroke. 2019;50(12).
120. Ritter S. Monitoring and Maintenance of Brain Glucose Supply: Importance of hindbrain catecholamine neurons in this multifaceted task. In: Harris RBS, editor. Appetite and Food Intake: Central Control[M]. 2nd ed. Boca Raton (FL): CRC Press/Taylor & Francis, 2017.
121. Freeman J. Management of hypoglycemia in older adults with type 2 diabetes[J]. Postgrad Med. 2019;131(4):241-250.
122. Bergmann M, Beer R, Kofler M, Helbok R, Pfausler B, Schmutzhard E. Acyclovir resistance in herpes simplex virus type I encephalitis: a case report [published correction appears in J Neurovirol. 2017 Jun 29;:][J]. J Neurovirol. 2017;23(2):335–337.
123. Tsuboguchi S, Wakasugi T, Umeda Y, Umeda M, Oyake M, Fujita N[J]. Rinsho Shinkeigaku. 2017;57(7):387–390.
124. Rico M, Martinez-Rodriguez L, Larrosa-Campo D, Calleja S. Dilemma in the emergency setting: hypomagnesemia mimicking acute stroke[J]. IMCRJ. June 2016:145.
125. Ropper AH. Neurosyphilis[J]. N Engl J Med. 2019 Oct 3;381(14):1358-1363.
126. Khaja M, Adler D, Lominadze G. Expressive aphasia caused by Streptococcus intermedius brain abscess in an immunocompetent patient[J]. Int Med Case Rep J. 2017;10:25-30.
127. Sun M, Herrmann N, Shulman KI. Lithium toxicity in older adults: a Systematic review of case reports[J]. Clin Drug Investig. 2018;38(3):201-209.
128. Hommers L, Fischer M, Reif-Leonhard C, Pfuhlmann B, Deckert J, Unterecker S. The combination of lithium and ACE inhibitors: Hazardous, critical, possible?[J]. Clinical drug investigation. 2019;39(5):485-9.
129. Altun İK, Kılıç N, Yıldızoğlu E, Atagün Mİ. Lithium associated side effects and neurotoxicity: Is lithium neurotoxicity related to iron deposition?[J]. Psikiyatride Guncel Yaklasimlar. 2019;11(2):141-53.
130. Madhusoodanan S, Reddy V, Mohan S. Intermittent transient motor aphasia associated with acute lithium toxicity: A case report and brief review[J]. Curr Drug Saf. 2017;12(3):201–204.
131. Payne LE, Gagnon DJ, Riker RR, Seder DB, Glisic EK, Morris JG, Fraser GL. Cefepime-induced neurotoxicity: a systematic review[J]. Crit Care. 2017;21(1):276.
132. Patel J, Hayes B, Bauler L, Mastenbrook J. Neurologic acyclovir toxicity in the absence of kidney injury[J]. J Emerg Med. 2019;57(2):e35-e39.
133. Liberman AL, Prabhakaran S. Stroke chameleons and stroke mimics in the emergency department[J]. Curr Neurol Neurosci Rep. 2017;17(2):15.
134. Vilela P. Acute stroke differential diagnosis: Stroke mimics[J]. Eur J Radiol. 2017;96:133–144.
135. Moulin S, Leys D. Stroke mimics and chameleons[J]. Curr Opin Neurol. 2019;32(1):54–59.
136. Yew KS, Cheng EM. Diagnosis of acute stroke[J]. Am Fam Physician. 2015;91(8):528–536.
137. Ralston SH, Penman ID, Strachan MW, Hobson R, editors. Davidson's principles and practice of medicine e-book[M]. Elsevier Health Sciences, 2018 .
138. Field K, Gharzai L, Bardeloza K, Houghton B. Takayasu arteritis presenting as embolic stroke[J]. BMJ Case Reports. August 2017:bcr-2017-220001
139. Sonneville R, Ruimy R, Benzonana N, et al. An update on bacterial brain abscess in

immunocompetent patients[J]. Clin Microbiol Infect. 2017;23(9):614–620.
140. Hussin S, Yusoff SSM, Zin FM, Ghani ARI. Frontal meningioma with psychiatric symptoms[J]. J Family Med Prim Care. 2018;7(1):252–254.
141. Robinson G, Blair J, Cipolotti L. Dynamic aphasia: an inability to select between competing verbal responses?[J]. Brain: a journal of neurology. 1998;121(1):77-89.
142. Buchwald A, Falconer C, Rykman-Peltz A, et al. Robotic arm rehabilitation in chronic stroke patients with aphasia may promote speech and language recovery (but effect Is not enhanced by supplementary tDCS)[J]. Front Neurol. 2018;9:853.
143. Duncan ES, Small SL. Changes in dynamic resting state network connectivity following aphasia therapy[J]. Brain Imaging and Behavior. 2018;12(4):1141-1149