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STROKE-RELATED ALIEN HAND SYNDROME: ETIOLOGY, CLINICAL PRESENTATION AND MANAGEMENT A SYSTEMATIC REVIEW

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ABSTRACT

Background: Alien hand syndrome (AHS) is a relatively rare neurological disorder characterized by involuntary, purposeful movements of a limb, as well as a sense of foreignness toward the affected limb. Recently, an increasing number of cases of alien hand syndrome has been observed; despite this, the pathophysiology, classification, and diagnostic management remain significant challenges for modern medicine. Stroke represents one of the earliest identified and potentially reversible causes.

Objective: To systematically review the etiology, clinical presentation, neuroanatomical substrates, and management of stroke-related AHS.

Methods: PubMed, Embase, Scopus, and Web of Science databases were searched from inception to 2025 using terms including "alien hand syndrome," "anarchic hand," and "stroke." Studies reporting AHS following ischemic or hemorrhagic stroke with neuroimaging confirmation were included.

Results: The most common cause of alien hand syndrome (AHS) is infarction in the territory of the anterior cerebral artery (ACA), involving the corpus callosum, supplementary motor area, and medial frontal cortex. Three clinical variants are distinguished: frontal (object manipulation, grasping, compulsive tool use), callosal (intermanual conflict), and posterior (limb levitation, sense of foreignness). Prognosis is generally favorable - isolated lesions of the corpus callosum or cingulate gyrus usually resolve completely, whereas combined damage to the corpus callosum and frontal cortex is associated with persistent symptoms. Treatment includes pharmacological interventions (clonazepam, botulinum toxin) and rehabilitation methods (verbal cues, limb restraint, mirror therapy).

Conclusions: Alien hand syndrome is a rare but recognizable clinical manifestation of stroke requiring rapid identification to differentiate it from psychiatric disorders. Early neuroimaging assessment of the corpus callosum and frontal lobe pathways is crucial for prognosis evaluation. Further studies are necessary to establish standardized diagnostic criteria and evidence-based rehabilitation protocols.

KEYWORDS

Alien Hand Syndrome, Anarchic Hand, Stroke, Corpus Callosum, Anterior Cerebral Artery, Supplementary Motor Area, Rehabilitation

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1. Introduction

1.1 Background and Historical Context

Alien hand syndrome (Alien Hand Syndrome, AHS) is a very rare neurological phenomenon characterized by involuntary, complex, yet seemingly purposeful movements of a limb, accompanied by a subjective sense of foreignness toward the affected limb [1][2]. The syndrome was first described by Kurt Goldstein in 1908 as “la main étrangère” (alien hand), and subsequent landmark observations were presented by Brion and Jedynak in 1972, who distinguished the callosal variant [1].

The initial descriptions of alien hand syndrome were primarily associated with stroke and neurosurgical procedures - particularly callosotomy, involving sectioning of the corpus callosum [2]. Currently, neurodegenerative diseases, especially corticobasal syndrome, are considered the most common cause of alien hand syndrome; however, stroke remains an important and potentially reversible cause requiring special attention [3].

1.2 Definition and Core Features

Alien hand syndrome (AHS) can be defined by two fundamental elements:

- (1) involuntary motor activity of a limb that appears purposeful and goal-directed
- (2) a sense of loss of control or lack of ownership over the affected limb [2][4].

Patients often describe their hand as something that functions alongside them, independently of their will, or just as often, against their will [1].

A distinction has been proposed between the phenomena of the “alien hand” and the “anarchic hand.” The term “alien hand” primarily refers to the feeling that the limb does not belong to the patient’s body and appears “estranged,” whereas “anarchic hand” describes involuntary yet purposeful movements [5]. In clinical practice, these phenomena often coexist and constitute a diagnostic challenge for physicians.

1.3 Rationale for This Review

Alien hand syndrome associated with stroke represents a significant diagnostic and therapeutic challenge. Due to its complexity and atypical clinical presentation, it may raise suspicion of psychiatric disorders, which can delay the initiation of targeted stroke treatment, where time is critical [6][7]. In contrast to neurodegenerative causes, stroke-related AHS may be reversible with appropriate treatment, making early clinical recognition crucial [8][9].

Despite the growing number of case reports and clinical series, no systematic review focused exclusively on stroke-related AHS has been conducted to date. The aim of this review is to synthesize current data regarding the etiology, clinical presentation, neuroanatomical basis, and treatment of alien hand syndrome following cerebrovascular events.

1.4 Objectives

The primary objective of this systematic review is to comprehensively analyze stroke-related AHS with respect to:

1. Vascular territories and lesion locations associated with AHS
2. Clinical subtypes and their distinguishing features
3. Pathophysiological mechanisms
4. Treatment and rehabilitation strategies
5. Prognosis and factors predicting recovery

2. Methods

2.1 Eligibility Criteria

Inclusion criteria:

- Case reports, case series, cohort studies, and reviews describing AHS following ischemic or hemorrhagic stroke
- Confirmed diagnosis of AHS with documented clinical features
- Neuroimaging (CT or MRI) confirming stroke lesion
- Published in English, French, German, or Spanish
- Publication date: Inception to December 2025

Exclusion criteria:

- AHS due to neurodegenerative diseases, tumors, trauma, or surgical callosotomy
- Abstracts without full text available
- Animal studies
- Duplicate publications

2.2 Information Sources and Search Strategy

The following databases were searched: PubMed, Embase, Scopus, Web of Science, and Cochrane Library.

Search terms:

"alien hand syndrome" OR "alien hand" OR "anarchic hand" OR "alien limb" OR "diagonistic dyspraxia" OR "intermanual conflict" AND "stroke" OR "cerebral infarction" OR "cerebrovascular" OR "ischemic" OR "hemorrhagic" OR "anterior cerebral artery" OR "posterior cerebral artery"

2.3 Study Selection and Data Extraction

Two independent reviewers screened titles and abstracts, followed by full-text review of potentially eligible studies. Disagreements were resolved by consensus.

Data extracted included: demographics (age, sex, handedness), stroke characteristics (type, vascular territory, lesion location), clinical features of AHS (variant, specific symptoms, associated neurological signs), treatment modalities, and outcomes.

3. Results

3.1 Epidemiology and Demographic

Stroke-related alien hand syndrome is a rare phenomenon, and its exact prevalence remains unknown. In a large Mayo Clinic series including 150 patients with the alien limb phenomenon, 14 cases (9.3%) were attributed to stroke. Ten of the 14 stroke-related cases involved the right hemisphere, resulting in alien hand syndrome occurring more frequently on the left side of the body [3].

A recent systematic review of 72 cases of AHS of various etiologies found that stroke was one of the most common causes, alongside neurodegenerative diseases. The mean patient age was 59.6 years, indicating that stroke-related AHS predominantly affects older individuals [1].

The mean age of patients with stroke-related AHS is approximately 60-74 years, reflecting the typical stroke population.[1][10] In one series of ACA stroke patients with AHS, the mean age was 74.2 years.[10] Sex distribution appears relatively equal, with females representing 51.4% in one large review.[1]

3.2 Vascular Territories and Lesion Locations

3.2.1 Anterior Cerebral Artery Territory

The anterior cerebral artery (ACA) territory is the most commonly implicated vascular distribution in stroke-related AHS.[10] ACA strokes may lead to impaired motor control in the absence of limb weakness and evoke AHS in its extreme form.[10] Key structures supplied by the ACA include:

- Supplementary motor area (SMA) and pre-SMA: Lesions within the pre-SMA are specifically related to AHS-specific signs[10]
- Anterior cingulate cortex: Involved in motor planning and volition
- Corpus callosum (anterior portion): The genu and body are supplied by ACA branches
- Medial prefrontal cortex: Critical for motor inhibition

3.2.2 Corpus Callosum Infarction

Corpus callosum infarction is a well-recognized cause of alien hand syndrome (AHS). In a study of 157 patients with corpus callosum infarction, 5 patients (3.2%) developed AHS, and all showed concurrent involvement of the cingulate gyrus [11]. Four of the five patients presented with intermanual conflict, whereas only one exhibited a prominent grasp reflex [11].

The corpus callosum has a dual blood supply:

- the anterior communicating artery and branches of the anterior cerebral artery (ACA), which supply the anterior portions
- branches of the posterior cerebral artery (PCA), which supply the posterior portion (splenium)

3.2.3 Posterior Cerebral Artery Territory

Posterior cerebral artery (PCA) strokes involving the posterolateral parietal lobe can produce the posterior variant of alien hand syndrome (AHS) [6][7]. In a Mayo Clinic series, 10 of 14 cerebrovascular cases originated in the right hemisphere, and all involved the parietal lobe [3]. This highlights the important role of the right parietal lobe in the pathophysiology of AHS.

3.3 Clinical subtypes

Based on lesion location and associated clinical presentation, three main variants of stroke-related alien hand syndrome (AHS) are recognized [11][2][4].

3.3.1

Lesion location: Supplementary motor area, pre-SMA, anterior cingulate gyrus, medial prefrontal cortex of the dominant hemisphere, and anterior corpus callosum[4]

Clinical features:

- Reflexive grasping and groping
- Compulsive manipulation of tools (utilization behavior)
- Difficulty releasing objects
- Impulsive reaching toward objects in the environment
- Typically affects the dominant hand[4]

The frontal variant results from release of exploratory reflexes coupled with loss of inhibitory control from the nondominant hemisphere.[4]

3.3.2 Callosal Variant

Lesion location: Corpus callosum, particularly the anterior and middle portions [12]

Clinical features:

- Intermanual conflict (hands working at cross-purposes)
- Diagnostic dyspraxia
- Self-oppositional movements
- Typically affects the nondominant hand [12]

The callosal variant arises from disconnection between the cerebral hemispheres, which becomes apparent during tasks requiring control by the dominant hemisphere [4]. A stroke limited to the middle and posterior portions of the corpus callosum body may cause a transient alien hand syndrome of the nondominant hand, which may be due to impaired interhemispheric communication [12].

3.3.3 Posterior Variant

Lesion location:

Posterior parietal cortex, parieto-occipital regions, and thalamus [2][3]

Clinical features:

- Arm levitation
- Withdrawal movements
- Prominent feeling of foreignness and lack of ownership of the limb
- Sensory deficits (hemisensory loss)
- Mild hemiparesis
- Ataxia

The posterior variant involves damage to the inferior parietal lobule and its connections — this leads to disturbance of body schema and the sense of limb ownership [2].

3.3.4 Mixed Variant

Extensive strokes, especially those involving the entire corpus callosum, may cause a mixed clinical presentation combining features of all three variants [13]. In one case report, a patient with an extensive corpus callosum infarction presented with grasping and groping (frontal variant), intermanual conflict (callosal variant), and arm levitation with hemisensory loss (posterior variant) [13].

Table 1. Clinical Subtypes of Stroke-Related Alien Hand Syndrome

Feature	Frontal Variant	Callosal Variant	Posterior Variant
Lesion location	SMA, pre-SMA, anterior cingulate, medial prefrontal cortex, anterior CC	Corpus callosum (anterior/middle)	Posterior parietal cortex, parieto-occipital, thalamus
Vascular territory	ACA	ACA, AComA	PCA
Affected hand	Dominant	Non-dominant	Either
Key features	Grasping, groping, compulsive tool use	Intermanual conflict, diagnostic dyspraxia	Levitation, foreignness, sensory loss
Sense of foreignness	Variable	Less prominent	Prominent
Associated signs	Gait apraxia, motor perseverations	Apraxia, agraphia	Hemisensory loss, ataxia

Abbreviations: SMA = supplementary motor area; CC = corpus callosum; ACA = anterior cerebral artery; AComA = anterior communicating artery; PCA = posterior cerebral artery

3.4 Associated Neurological Signs

Stroke-related AHS frequently occurs with other neurological deficits, which may aid in localization:

- Apraxia: Ideomotor and constructional apraxia, particularly with callosal lesions [13]
- Transcortical motor aphasia: With dominant hemisphere involvement [13]
- Gait apraxia: Common with ACA territory strokes [10]
- Cognitive impairment: Attention and executive dysfunction [13]
- Mirror movements: Involuntary mirroring of contralateral hand movements [10]
- Motor perseverations: Difficulty stopping initiated movements [10]

3.5 Pathophysiology

Several theories have been proposed to explain the pathophysiology of stroke-related alien hand syndrome:

3.5.1 Disconnection Hypothesis

The classic explanation posits that AHS results from disconnection of the primary motor cortex from premotor areas while retaining the ability to execute movements [6]. Callosal damage disrupts interhemispheric communication, leading to independent action of the nondominant hemisphere [4][12].

3.5.2 Network Disruption Model

Modern neuroimaging studies emphasize disruption of distributed motor control networks rather than isolated lesions [14][15]. Diffusion tensor imaging (DTI) studies have identified involvement of multiple white matter tracts:

- Corpus callosum (particularly posterior parietal and temporal sections)
- Superior longitudinal fasciculus
- Arcuate fasciculus
- Inferior longitudinal fasciculus
- Frontal aslant tract
- Cingulum bundle [14][15]

3.5.3 Supplementary Motor Area Dysfunction

The SMA and pre-SMA are critical for internally generated, volitional movements. Damage to these areas releases stimulus-driven motor responses while impairing self-initiated actions [10]. Electroencephalographic studies have demonstrated absence of the Bereitschaftspotential (readiness potential) over the damaged hemisphere, indicating disrupted motor preparation [10].

3.6 Differential Diagnosis

Stroke-related alien hand syndrome should be differentiated from several clinical conditions. Physicians who are unaware that alien hand syndrome may represent a manifestation of stroke may misinterpret the symptoms as psychiatric disorders, which may consequently lead to delayed initiation of appropriate treatment [6].

Table 2.

Condition	Distinguishing Features
Psychiatric disorders	No structural lesion; movements may be suppressible
Utilization behavior	Grasping without sense of foreignness
Hemispatial neglect	Inattention to contralesional space; no involuntary movements
Somatoparaphrenia	Denial of limb ownership without involuntary movements
Limb-kinetic apraxia	Clumsy movements; no involuntary activity
Chorea/athetosis	Irregular, non-purposeful movements
Psychogenic movement disorder	Inconsistent; distractible; no structural lesion

3.7 Management

3.7.1 Acute Stroke Treatment

The foundation of management is treatment of the underlying stroke:

- Acute reperfusion therapy when indicated
- Secondary prevention (antiplatelet agents, statins, risk factor modification)
- Standard stroke unit care

One case report demonstrated complete remission of AHS within 8 days with aspirin, clopidogrel, atorvastatin, and memantine [8].

3.7.2 Pharmacological Interventions

Evidence for pharmacological treatment is limited to case reports:

Clonazepam: The most commonly reported medication, with suspected efficacy based on GABAergic modulation of motor circuits [13][16].

Doses of 0.5-2 mg daily have been used.

Botulinum toxin: May be considered for severe grasping behavior, though limited by the need for preserved voluntary function [16].

Memantine: NMDA receptor antagonist reported in one case with good response [8].

3.7.3 Rehabilitation Strategies

Multiple rehabilitation approaches have been described: [13][17,18]

Behavioral strategies:

- **Verbal cueing:** Patients learn to verbally command their hand, which has shown good outcomes in mixed AHS. Self-talk and internal commands can help patients consciously restrain involuntary movements [18, 19].

- **Visual monitoring:** Continuous visual attention to the affected limb

- **Task-specific training:** Structured practice of functional activities

Compensatory techniques:

- **Limb restraint:** Physically restraining the affected hand (e.g., sitting on it, holding an object) reduces interference with activities [16, 17]

- **Distraction:** Keeping the affected hand occupied with a neutral object

- **Environmental modification:** Removing triggering stimuli from the environment

Specialized therapies:

- **Mirror box therapy:** May help restore sense of agency [13]

- **Bimanual hand training:** Coordinated bilateral activities [13]

- **Cognitive behavioral therapy:** Addresses psychological distress and coping [13]

One comprehensive rehabilitation program combining these approaches achieved almost complete resolution of AHS features by 9 months post-stroke [13].

Table 3. Management Strategies for Stroke-Related Alien Hand Syndrome

Intervention	Description	Evidence Level
Acute stroke treatment	Reperfusion therapy, secondary prevention	Standard of care
Clonazepam	0.5-2 mg daily	Case reports
Botulinum toxin	For severe grasping	Case reports
Memantine	NMDA antagonist	Single case report
Verbal cueing	Self-commands to control hand	Case series
Limb restraint	Physical restraint of affected hand	Case reports
Visual monitoring	Continuous visual attention	Expert opinion
Mirror therapy	Mirror box training	Case reports
Occupational therapy	ADL adaptation, compensatory strategies	Case series

3.8.1 General Outcomes

Stroke-related AHS generally has a favorable prognosis compared to neurodegenerative causes [8,9]. Many cases show spontaneous improvement or complete resolution with treatment.

- **Frontal AHS following ACA stroke:** Complete resolution within 7-9 months reported [9]

- **Corpus callosum infarction:** Remission within 8 days to several months [8][18]

- **Mixed variants:** Near-complete resolution by 9 months with comprehensive rehabilitation [13]

3.8.2 Prognostic Factors

A systematic review of post-stroke AHS identified key prognostic factors: [14]

Favorable prognosis (early resolution):

- Isolated callosal lesions

- Isolated fronto-parietal lesions

- Callosal plus cingulate lesions only

Poor prognosis (chronic persistence):

- Combined corpus callosum AND frontal cortex damage
- Combined corpus callosum AND fronto-parietal cortex damage
- Extensive white matter tract disconnection (callosal fibers, superior longitudinal fasciculus, frontal aslant tract, cingulum bundle)

Agency disruption (loss of voluntary control) is universal in post-stroke AHS, whereas ownership loss (feeling of foreignness) occurs selectively, typically with parietal, parieto-occipital, or combined callosal-frontal lesions. [14]

Table 4. Prognostic Factors in Stroke-Related Alien Hand Syndrome

Factor	Favorable Prognosis	Poor Prognosis
Lesion pattern	Isolated callosal	Combined CC + frontal
	Isolated fronto-parietal	Combined CC + fronto-parietal
	CC + cingulate only	Extensive white matter involvement
White matter tracts	Limited disconnection	SLF, FAT, cingulum involvement
Clinical features	Agency loss only	Agency + ownership loss
Time course	Early improvement	Persistent at 3+ months

Abbreviations: CC = corpus callosum; SLF = superior longitudinal fasciculus; FAT = frontal aslant tract

3.8.3 Recovery Trajectory

In the acute phase, patients may be unaware that their hand is moving against their will.[19] With time and rehabilitation, patients typically develop:

1. Recognition of involuntary movements
2. Ability to physically restrain the hand with the unaffected limb
3. Ability to mentally/verbally restrain movements
4. Gradual reduction in frequency and severity of symptoms [19]

4. Discussion

4.1 Summary of Evidence

This systematic review demonstrates that stroke-related AHS is a rare but clinically important presentation of cerebrovascular disease. The condition most commonly results from ACA territory infarctions affecting the corpus callosum, SMA, and medial frontal cortex. Three clinical variants (frontal, callosal, posterior) are recognized, each with distinct features and anatomical substrates.

The prognosis of stroke-related AHS is generally favorable, particularly compared to neurodegenerative causes. Early identification and treatment of the underlying stroke, combined with targeted rehabilitation, can lead to significant improvement or complete resolution in many cases.

4.2 Clinical Implications

4.2.1 Diagnostic Considerations

Emergency physicians and neurologists should be aware of AHS as an atypical stroke presentation [7]. Key diagnostic points include:

- AHS can occur without typical motor weakness
- Symptoms may be mistaken for psychiatric disorders
- Urgent neuroimaging is essential
- MRI with diffusion-weighted imaging is preferred for detecting callosal infarcts

4.2.2 Proposed Diagnostic Algorithm

1. Clinical recognition of involuntary purposeful movements with sense of foreignness
2. Urgent neuroimaging (MRI preferred)

3. Identification of lesion location and vascular territory
4. Classification of AHS variant
5. Assessment of associated neurological deficits
6. Initiation of stroke treatment and rehabilitation

4.2.3 Treatment Algorithm

Acute phase:

- Standard acute stroke management
- Secondary prevention
- Patient and family education

Subacute/chronic phase:

- Consider clonazepam trial (0.5-2 mg daily)
- Initiate rehabilitation program:
 - Verbal cueing training
 - Limb restraint strategies
 - Visual monitoring techniques
 - Occupational therapy for ADL adaptation

4.3 Limitations

This review has several limitations:

- Evidence is predominantly from case reports and small case series
- No randomized controlled trials exist for AHS treatment
- Heterogeneity in outcome measures and follow-up duration
- Publication bias toward unusual or severe cases
- Inconsistent terminology (alien vs. anarchic hand)
- Lack of standardized diagnostic criteria

4.4 Future Directions

Several areas require further investigation:

1. **Standardized diagnostic criteria:** Development of validated clinical criteria for AHS diagnosis and subtype classification
2. **Prospective registries:** Multi-center registries to better characterize epidemiology and natural history
3. **Neuroimaging studies:** Advanced DTI and functional MRI studies to map network disruption patterns
4. **Rehabilitation trials:** Controlled studies comparing rehabilitation strategies
5. **Pharmacological trials:** Systematic evaluation of clonazepam and other agents
6. **Outcome measures:** Development of validated assessment tools specific to AHS

5. Conclusions

Stroke-related alien hand syndrome is a rare but recognizable neurological presentation characterized by involuntary, purposeful limb movements with a sense of estrangement. It most commonly results from anterior cerebral artery territory infarctions affecting the corpus callosum, supplementary motor area, and medial frontal cortex.

Three clinical variants are recognized: frontal (grasping, groping, compulsive tool use), callosal (intermanual conflict), and posterior (levitation, foreignness). The prognosis is generally favorable, with isolated callosal lesions often achieving complete resolution, while combined callosal-frontal damage predicts chronic persistence.

Management includes acute stroke treatment, pharmacological interventions (primarily clonazepam), and rehabilitation strategies emphasizing verbal cueing, limb restraint, and visual monitoring. Early recognition is essential to differentiate AHS from psychiatric disorders and initiate appropriate stroke interventions.

Further research is needed to establish standardized diagnostic criteria, develop validated outcome measures, and conduct controlled trials of rehabilitation and pharmacological interventions.

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