

**ALIEN HAND SYNDROME - A MINI REVIEW**

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**ABSTRACT**

Alien hand syndrome (AHS) also called as Dr. Strangelove syndrome or anarchic hand is autonomous, motor, involuntary movement of limb. It is caused when a person had two brain hemispheres surgically separated, as seen in epilepsy, psychosis, migraine, parkinsonism, Creutzfeldt Jacob disease, HIV, tumor etc. This disorder is associated with frontal, occipital and parietal lobes of brain. Any damage to these lobes results in prior activation of primary motor cortex, disconnection between hemispheres of brain and loss of inhibitory control in pre motor system which results in uncoordinated movements of afflicted limb. AHS can be diagnosed by using neuroimaging techniques like FMRI, FDG-PET, DTT, rCBF using SPECT. AHS can be treated through direct physical interventions such as by using of cane, drugs like Clonazepam, botulinum toxin (butox) and visualization strategies.

**KEYWORDS:** Alien hand syndrome, involuntary movement, pre motor cortex, neuroimaging, Butulinum.**INTRODUCTION**

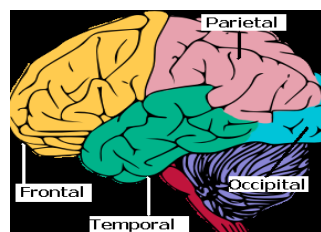
Alien Hand Syndrome is also known as Dr. Strangelove syndrome.<sup>[1]</sup> Strangelove hand or anarchic hand is a high order, autonomous, motor control activity neurological disorder.<sup>[2]</sup>

It is perceived as an involuntary, yet purposeful movements of limbs.<sup>[3]</sup> In AHS the hands are commonly affected (typically the left hand) and rarely the leg. If the leg is affected, then it is called as Alien limb phenomena (ALP). AHS remain a rare disorder caused mainly due to neurological disorders. These mainly affects brain, spinal cord and nerves. These disorders have wide range of causes including bacterial, viral, fungal and parasitic. For Example, infection by Plasmodium parasites cause malaria which often leads to spinal cord disorders leading to irreparable damage such as immunosuppressive activity.

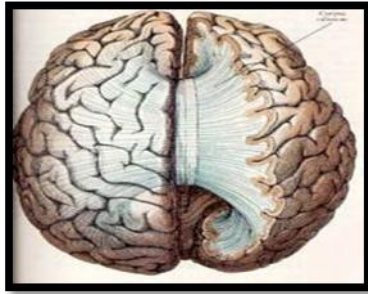
In common neurological disorders such as epilepsy in which the individual constantly experiences seizures, Alzheimer's disease in which individuals undergo mental deterioration and suffer from memory loss and cerebrovascular diseases such as migraines, strokes and much more. Neurological disorder like multiple sclerosis which is an auto immune disorder affects the myelin sheath covering of nerves, is less prone to AHS, on the other hand individuals suffering from parkinsonism and brain tumors are more prone to AHS. These neurological

disorders are common worldwide, with millions of individuals affected.

AHS is an autonomous condition in which an individual's limb is affected which performs purposeful action without any intension and control. Sometimes, the affected limb interferes with the normal actions of other unaffected limbs. Furthermore, the afflicted individual reach for objects and manipulate them without any intensions to do so, even if the point is to use the controllable hand for restraining the alien hand. In AHS there is a complex sense of limb foreignness including misidentifying the limb as the examiners. Sometimes the affected limb is so personified that the patients have named their alien hands.<sup>[4]</sup> The areas of the brain that are associated with AHS are the frontal, occipital and parietal lobes as shown in Figure 1.

**Figure 1: Areas of Brain affected in ALS.**

AHS is best documented in cases where a person has the two hemispheres of their brain surgically separated as shown in Figure 2.



**Figure 2: Surgically separated brain hemispheres.**

It is seen in the extreme cases of epilepsy and epileptic psychosis, e.g., temporal lobe epilepsy.<sup>[5]</sup> AHS also occurs in some cases after brain surgery, stroke<sup>[3]</sup>, infection, Pneumocephalus<sup>[6]</sup>, Parry-Romberg syndrome, progressive hemifacial atrophy<sup>[7]</sup>, tumor, Gun Shot Wound<sup>[8]</sup>, aneurysm, migraine<sup>[9]</sup>, HIV<sup>[10]</sup> and specific degenerative brain conditions such as Alzheimer's disease and Creutzfeldt–Jakob disease and parkinsonism disease.<sup>[11]</sup>

### SIGNS AND SYMPTOMS

Alien hand condition is differentiated from reflexive behavior where the former is purposive and the latter is obligatory. There is a clear difference between the behaviors of the two hands i.e. normal hand and the alien hand. The Alien hand is generally "disobedient" and viewed as "wayward" whereas the unaffected hand is under normal voluntary condition.

In some cases where the damage occurs to the corpus callosum, the hands appear to act opposite to each other and this is known as "utilization behavior". It is mostly associated with bilateral frontal lobe and depends on the surrounding environmental indicators to guide the alien hand. This condition is referred as "environmental dependency syndrome".<sup>[12]</sup>

The main symptoms which are observed in majority of afflicted person are

- Lack of awareness of arms involuntary movements or actions
- Lack of control over arm movements
- Inability to feel control over hand movements

### HISTORICAL OVERVIEW

- Kaiser in 1897, described about unilateral apraxia and disinhibited grasp reflex after cerebral injury. This was later explained by Liepmann in 1990.<sup>[13]</sup>
- Van Vleuten in 1907 described about the patients who acquired complex movement disorder due to left hemisphere brain tumor that had invaded the corpus callosum.<sup>[14]</sup>
- AHS was first described in 1908 by Kurt Goldstein, a German neuropsychiatric. He reported that a right-

handed patient with stroke developed involuntary actions of left-hand. Here, the individual reported that the limb moves on its own, performs repetitive involuntary grasping.<sup>[15]</sup>

- In succeeding years, such acquired complex behavior was recognized by different terms like, "pseudo spontaneous movements", Nachgreifen ("after-grasping"), "magnetic apraxia", "manual grasping behavior", the "groping-grasping reaction" and "visual groping".<sup>[2]</sup>
- In 1972, Brion and Jedynak were the first to coin the term "alien hand" after observing three patients with callosal tumor who were unable to recognize their own hands.<sup>[16]</sup>

### CAUSES OF AHS

- Influencing of pre- motor cortex prior to primary motor complex.
- Disconnection between different parts of brain.
- Loss of inhibitory control in premotor system.
- Disconnection of hemispheres due to injury.

### Influencing of primary motor cortex prior to pre-motor complex

In voluntary actions, the agency system which seems to be associated with voluntary movement appears to be followed with a sequential activation of premotor cortex (generates neuronal impulse) before activation of the primary motor cortex (execution of the movement) then, the hand movement is being generated.

But in case of Alien hand the primary motor cortex gets priorly activated before premotor cortex. As a result, "sense of agency" that is generally associated with voluntary movement is impaired or lost. This results in direct action or movement of the limb without any such intentions.<sup>[17]</sup>

### Disconnection between different parts of Brain

Different regions of brain are responsible for different functioning. Surgically separated brain hemispheres lead to disconnection between different parts of brain, resulting in AHS. This is because different regions of the brain are able to command movements, but cannot generate a conscious feeling of self-control over these movements.

Thus, the agency system which is associated with voluntary movement is impaired or lost.

### Loss of Inhibitory control in premotor system

The brain has distinguished "premotor" also called as "agency" systems which transform intentions into overt actions. An anteromedial frontal premotor system directs examining actions by affecting the inhibitory control over such actions. Whereas the Posterolateral parieto-occipital has an inhibitory control over the voluntary tasks as well as the involuntary actions depending on external stimulation.

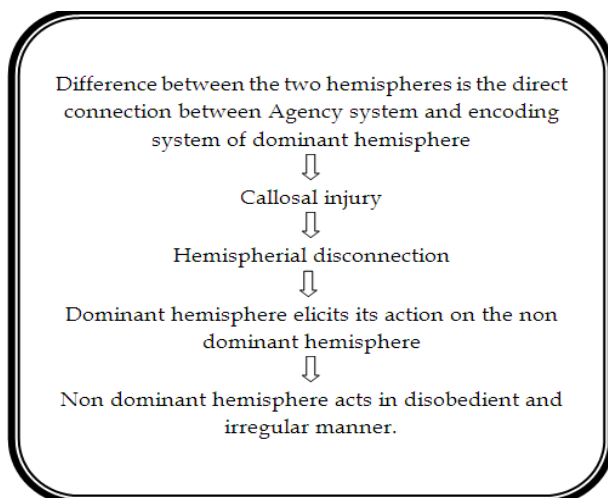
These two systems are termed as intrahemispheric systems. These systems maintain a balance between approaching towards and withdrawing from the environmental stimuli. These two systems develop an integrated trans-hemispheric agency system. The damage to these system results in positive and negative cortical tropism which is described by Denny brown.<sup>[18]</sup>

Damage to anteromedial frontal system causes, involuntary but purposive movements of an exploratory reach-and-grasp nature (positive cortical tropism).

The damage in the posterolateral parieto-occipital system, results in involuntary purposive actions of a release-and-retract nature, such as levitation and instinctive avoidance (negative cortical tropism). In both, the affected actions are released in contralateral limb. Incomplete bihemispheric suppression leads to involuntary hand movements. Electrophysiology studies support this disinhibition.

### Disconnection of Hemispheres Due to Injury

The main difference among the two hemispheres is direct link between two systems of dominant hemisphere. Injury in the corpus callosum (responsible for primary control) results in hemispherical disconnection. Upon which the dominant hemisphere elicits its action on nondominant hemisphere resulting in disobedient manner of limb as shown in Figure 3.



**Figure 3: Flow Chart showing Disconnection of hemispheres due to callosal injury.**

The affected regions of brain in AHS results in different phenomenological variations. Depending upon the severity of variations they are classified into three variants i.e., Anterior and posterior and mixed variants. Each variant has different characteristics and distinguishing features.

### ANTERIOR VARIANT

Lesions of Supplementary motor area (SMA), Cingulate cortex, dominant medial prefrontal complex or callosum results in anterior variants.

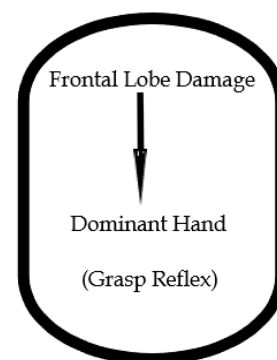
The anterior variants are further classified into two subtypes depending upon the lesions.

1. Frontal variant
2. Callosal variant

### Frontal variant

Individual with the frontal variant exhibit groping, grasping and manipulation of nearby things. The frontal variant results from lesions of the supplementary motor area (SMA), cingulate cortex and dominant medial prefrontal cortex.

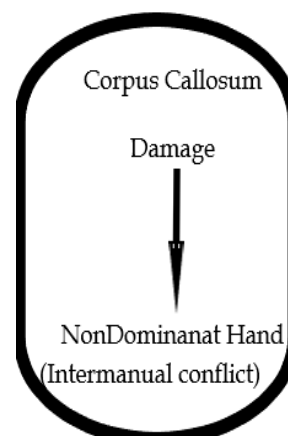
The frontal variant affects the dominant hand and alters the motor planning affecting the dominant hand. So, the affected dominant hand reaches towards and grasps objects which are shown in Figure 4.



**Figure 4: Frontal lobe injury in dominant hand.**

### Callosal variant

The callosal variant, particularly common with lesions to the anterior third of the rostrum. Mischievous actions interfering with tasks or removing desired objects are commonly evolved. Callosal lesions affect the non-dominant hand. The affected non dominant hand interferes with the tasks causing intermanual conflict<sup>[19]</sup> which is shown in Figure 5.



**Figure 5: Callosal injury in nondominant hand.**

### POSTERIOR VARIANT

A posterior variant result from thalamic, posterolateral parietal or occipital lobe damage. It is characterized by hemianesthesia, hemianopia, visuospatial neglect and

optic ataxia. It is particularly observed in different neurodegenerative conditions like parkinsonism disease, Alzheimer's disease or a tauopathy and progressive supranuclear palsy.<sup>[20]</sup>

The posterior variant is further classified into

1. Parietal variant
2. Occipital variant

The parietal variant results in unintentionally withdrawing the afflicted hand from environmental contact or stimuli (avoidance response). The occipital variant is accompanied by uncoordinated hand movements or involuntary levitation which may be task specific.<sup>[21]</sup>

The affected hand also has unusual signs and postures with the palmar surface restraining from approaching objects.

### MIXED VARIANTS

#### Mixed variants adding to the complexity of AHS

Sometimes, both the Anterior and Posterior variants get mixed and results in causing intermanual conflict present in left hand. In right hand groping and grasping behaviours, this is due to functional rearrangement of interhemispheric motor pathways.<sup>[22]</sup>

### DIAGNOSIS OF AHS

#### Structural and functional imaging techniques helps in diagnosing AHS

Functional imaging involves

- i. Diffusion tensor tractography (DTT)
- ii. FDG-PET
- iii. FMRI
- iv. Regional cerebral blood flow (rCBF) using single-photon emitted computed tomography (SPECT).

#### i). DTT

It is a 3D technique providing fiber tract visualization, shed light into the connectivity of the corpus callosum. DTT reveals significant disruption of callosal fibers.<sup>[23]</sup>

#### ii). FDG-PET

It is a medicine functional imaging technique which is involved in controlling and inhibiting an alien limb.<sup>[24]</sup>

#### iii). FMRI (Functional MRI) study

This study diagnoses the lesions in right parietal cortex caused due to callosal injury.<sup>[11]</sup>

This study helps in analyzing the correlation between parietal cortex activation and a task the individual performs during the scan.

#### v). Regional cerebral blood flow (rCBF) using single-photon emitted computed tomography (SPECT)

This study demonstrates the reduction in rCBF in the right parietal region, right thalamus, supramarginal gyrus and the posterior cingulate gyrus.<sup>[25]</sup>

### DISEASES CAUSING ALIEN HAND SYNDROME

#### Migraine

Migraine affects the physiology of cortical region and this change in physiology induce both ictally and interictally dysfunction, leading to alien hand syndrome.

#### Pneumocephalus

After successful surgery of pneumocephalus, the patient later may develop frontal space-occupying lesion resulting in alien hand syndrome.

#### Stroke

The stroke in the corpus callosum i.e., the parietal or frontal regions results in involuntary motor behaviors and further leading to object grasping and intermanual conflict.

#### Partial status epilepticus

Continuous spikes in the right frontotemporal region and manifestations of the actual seizure activity results in AHS.

#### Parry-Romberg Syndrome and Progressive Hemi facial Atrophy

Focal progressive atrophy and gliosis in the contralateral thalamus results in AHS due to unilateral damage of thalamus region.

#### HIV/AIDS

A midline deviation in intrahemispheric region, formed during a surgery leads to loss of control in the left hand with extra volition movements, groping unneeded objects, memory loss, hemineglect and dysphoria.

#### Gunshot Wound

A gunshot wound to the frontal lobes results in AHS.

#### Callosal Hemorrhage

A Callosal Hemorrhage in the medial frontal lobe leads to have both intermanual conflict and compulsive grasping movements.<sup>[23]</sup>

#### Parkinsonism

After successful surgery of Parkinsonism, the patient later may develop rapid loss of control in left hand resulting in alien hand syndrome.<sup>[11]</sup>

### TREATMENT

There are no approved or recommended therapies for AHS. Its management is based on pharmacologic, physical and behavioral interventions. Other way includes "muffling" the action of the alien limb by placing it in a restrictive "cloak" like specialized soft foam hand orthosis. An orthotic device is used to inhibit or restrict grasping or restraining the affected hand. The patient is trained to perform a specific task, in a particular environmental target.<sup>[26]</sup>

**Clonazepam**

It is used in the management of convulsions, panic disorder and akathisia i.e. movement disorder. It is a tranquilizer of the benzodiazepine class. Clonazepam reduces 70% of levitations (lifting objects unintentionally from the surroundings) per minute. It potentiates thalamic GABAergic neurons, which reduces the arm's oversensitivity to external stimuli or reduces the internal stimulus driving the AHS.

**Botulinum toxin**

Botulinum toxin type A is also called as Onabutilinum toxin A injection. This is made from the bacteria. It blocks nerve activity in the muscles. It inhibits the release of neurotransmitter acetyl choline from the axon endings at neuromuscular junction and reduces levitation.<sup>[27]</sup>

**CONCLUSION**

- In spite of the above therapies AHS is not easy to treat, because different parts of brain are damaged which leads to different behaviour and feelings.
- New techniques and pharmacologic interventions have to be discovered to manage such awful disorder.

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**CONFLICT OF INTEREST**

Authors do not have any conflict of interest with any individual and institution.

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