

Alien limb syndrome - A systematic literature review of rehabilitation strategies

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SUMMARY

Alien Limb Syndrome (ALS) is a neurological condition that is heavily characterized by involuntary coordinated motor activity in the limbs of the affected individual. They are majorly characterized by opposing movements in the limbs, Sudden Grasps (SGs), and Limb Elevations (LEs). Lesions in the medial frontal lobes, parietal lobes, and corpus callosum are the most prevalent causes of ALS. Since its awareness was heightened in 1964 following the popular movie by Stanley Kubrick, scientists, and health practitioners have experimented with using diverse rehabilitation therapies to correct this condition. These rehabilitation techniques include both pharmacological and physical therapies. However, there have been no clinical trials or standardized therapies adopted. This article reviewed 5 case studies with emphasis on the rehabilitation therapies used and their effectiveness. Pharmacological therapies, which include drugs such as botulinum, proved to drastically improve the patient's spontaneous LEs and sudden grasps SGs by 84% and 77% then clonazepam improved the LEs and SGs by 73% and 70% respectively. Physical therapies which involved eye-hand coordination showed good results.

Key words: Alien Limb Syndrome (ALS) – Neurological condition – Rehabilitation – Physical therapy – Pharmacological therapy

INTRODUCTION

Alien Limb Syndrome (ALS) is a neurological malfunction heavily characterized by involuntary coordinated motor activity in the limbs of the affected individual (Manea et al., 2024). It is frequently connected with lesions of parts of the brain (Litvan et al., 2003; Kikkert et al., 2006; Bartolo et al., 2011) It is also known as the “Dr. Strangelove syndrome” due to the awareness that the character Dr. Strangelove brings to the subject in a popular movie by Stanley Kubrick in 1964. Patients describe the syndrome as performing seemingly deliberate or semi-purposeful actions that occur independently of or notwithstanding their intentions (Wolpe et al., 2020). The affected limb is seen as ‘alien’ due to the inability of the individual to recognize the limbs as part of the body when taken out of plain sight or when the individual is blindfolded. The frontal and the right side of the parietal lobes, which are crucial in the way the human body is perceived by the brain, were proposed as the probable structural and functional

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Table 1. The Alien Limb Syndrome, commonly affected areas, causes and their types.

Type	Commonly affected Areas	Common Causes	Symptoms and Signs
Frontal	Supplemental motor area Cingulate gyrus Corpus Callosum	Tumors Infarction Trauma	Groping Gasping Utilization Behavior
Posterior	Parieto-occipital cortices Thalamus	Infarction Creutzfeld–Jakob disease Corticobasal syndrome	Levitation Cortical sensory deficits Abnormal limb posture

basis of these complicated involuntary functions (Tsakiris, 2010). Some clinical and behavioral characteristics might differ greatly from person to person. Some patients may be conscious of their involuntary motor activities immediately after the action occurs, while others may not be conscious of it until they are informed by someone (Biran, 2004).

Various clinical illnesses affect voluntary control but are not the same as alien limb syndrome (Kranick and Hallett, 2013). Psychogenic movement disorders, for example, might involve involuntary motions that are not caused by organic neuropathology. Typically, these are stereotyped motions (Hallett, 2010). Tics are involuntary movements or vocalizations that are partly independent of the patient’s willpower. Tics are stereotyped, and they may be repressed partially or temporarily with mental effort or by focusing on other tasks (Cohen et al., 2013). Choreiform motions are a series of involuntary, brief, migratory muscular contractions (Cardoso et al., 2006). Choreiform motions, unlike alien limbs, are unaffected by external stimuli. Xenomelia is an uncommon disease in which patients believe one or more of their limbs do not belong to them and, in some cases, seek a means of completely dissociating from the leg such as amputation (Brugger et al., 2013). Notably, this lack of ownership is not associated with involuntary movements and is more usually aligned with body dysmorphic disorder.

The etiology of Alien Limb Syndrome is thought to arise from diverse causes (Table 1). They are also shown to be prevalent in some neurological disorders such as corticobasal ganglionic degeneration, Alzheimer’s disease, brain tumors, and stroke. Lesions in the medial frontal lobes, parietal lobes (Goldberg and Bloom, 1990; Scepkowski and Cronin-Golomb, 2003), and the corpus

callosum are the most prevalent causes of Alien Limb Syndrome (Alfaro et al., 2017; Graff-Radford, 2013; Biran, 2004; Ay et al., 1998). Lesions and tumors in these different regions give rise to two variants of Alien Limb Syndrome; the Anterior and Posterior Variants. Injury to the frontal lobe and corpus callosum causes anterior variant Alien Limb Syndrome, whereas damage to the thalamus, parietal, and occipital lobe causes posterior variant ALS (Park et al., 2012; Kikkert, 2006; Dolaod et al., 1995).

REHABILITATION THERAPIES IN CLINICAL CASE STUDIES

Since the discovery of ALS, different rehabilitation therapies have been administered to patients. This article will focus on reviewing 5 published and reported case studies and their corresponding therapies in clinical treatment.

Since the first sighting of ALS by Goldstein in 1908 as “a form of apraxia identifiable by a sensation of estrangement and conflict that is present between the patient’s consciousness and his hand”, there has been no authorized or recommended treatments. The treatments are primarily built on anecdotal reports of pharmaceutical and behavioral strategies. Treatments that focus on the patient’s requirements are the most useful in terms of rehabilitation tactics. In this review, we will focus on the rehabilitation techniques applied in several cases

Case Study 1

Elendu et al. (2024) wrote a case report involving a 54-year-old male Caucasian who complained of involuntary movements of his left hand. Upon diagnosis, it was observed that the patient demonstrated involuntary actions that did not align with his intentions. He also demonstrated weak grip

strength and poor motor coordination in his left hand. It was determined at the end of the examinations that there was a lack of sync between intentions and actions in the patient's left hand. Physical examinations, neuroimaging, and clinical interviews were the diagnostic tools used. A few rehabilitation strategies were employed

- a. 500 mg Levetiracetam was administered twice daily and increased steadily over 3 months.
- b. Behavioral strategies to stop involuntary movements, mindfulness exercises, and cognitive strategies to refocus attention were applied for 3 months, followed by easing into normal daily activities.

After the duration of therapy, Mr. Anderson's motor control gradually improved, according to assessments by the clinicians. The alien hand motions became less frequent, which improved coordination when performing daily chores. The evaluation showed fewer mirror movements, which suggested that his right and alien left hands were more easily distinguished from one another.

Case Study 2

In 2004, Pappalardo et al. (2004) reported a case of a 60-year-old man who was primarily right-handed. He suffered an ischemic stroke caused by an obstruction of the left posterior cerebral artery. Following clinical assessment at the hospital, a significant right upper motor neuron facial paresis was revealed, as well as modest weakness in both the upper and lower limbs. Verbal understanding, repeating words, and concise reading, alongside item identification, visual coordination, and fine motor movements in both upper limbs, were considerably hindered.

The left cortical-subcortical parieto-occipital area was shown to have a suspected infarct on an initial brain CT without contrast. Three months following the stroke, a neurological test revealed that the right facial-brachial-crunal hemiparesis had fully recovered; understanding of words, repeating words, and concise reading, alongside item identification, visual coordination, and fine motor movements in both upper limbs, were all normal. When the motor behavior of the right upper arm was examined, it was found that there

was inter-manual conflict, infrequent involuntary synchronous movements during purposeful unilateral motions of the unaffected limb, and difficulties releasing things. His right arm and hand gave a feeling of body alienation, but he was unaware of this. His right hand felt handicapped.

Three months post-onset, a fresh brain MRI revealed a significant left cortical-subcortical parieto-occipital ischemia lesion. The neuropsychological assessment revealed substantial impairments in perception and spatial reasoning, as well as visual-spatial cognition deficits and constructive abnormalities. Physical Rehabilitation therapies were prescribed. They are as follows:

- a. Measure the length of ten distinct lines (10 challenges),
- b. Detect the spatial orientation of ten lines,
- c. Mentally rotate ten two-dimensional complicated geometric shapes,
- d. Identify ten complex figures,
- e. Identify ten hidden figures, and
- f. Mentally create ten complex figures (Pappalardo, 2004)

Rehabilitation began 3 months after the onset of the stroke (Hallett, 2001). The rehabilitative therapy lasted six months in total, with six sessions per week for the first month and three sessions per week for months two through six. When the patient was away from the rehabilitation setting, the injured arm was kept static at the back of the patient. Intermanual conflict (IMC) between the injured limb and the unaffected limb interfered with specific actions. Intermanual conflict was reduced as a result, and the patient was able to do numerous Activities of Daily Living (ADLs) using the non-affected arm.

Within the rehabilitative context, the training that focused on motor functions was strongly aimed at the afflicted limb. The use of the right arm (the affected arm) was gradually promoted in various ADLs after that. The physiatrist collaborated with the neurologist, neuropsychologist, therapist, and members of the patient's family to arrange rehabilitation. The family of the patient constantly communicated with the patient and

was able to offer helpful advice and recommendations on how to proceed. The rehabilitation therapy was tailored to the patient's specific needs.

As an outcome of the therapy, the patient acquired sufficient proficiency in the execution of various procedures which mirrored only everyday pursuits, eventually allowing him to handle efficiently kitchen and dining utensils with his right hand. His hand motor conduct was still sloppy and uncoordinated, even though his functional abilities had improved. Additionally, a specially made pen that was larger than a standard one helped him improve his ability to hold and squeeze. Over time, the patient's right hand's ability to write was restored. Wearing gloves allowed for easier tool manipulation, which was made easier by using smooth round tools. The patient was able to easily either catch or release the instruments.

There was no detection of obsessive tool manipulation or inter manual conflict in the follow-up assessment, which was conducted 24 months after the stroke. No further rehabilitative therapy was administered after the sixth month.

Case Study 3

In a case reported by Haq et al. in 2010, a 13-year-old girl was assessed, who showed signs of Alien Limb Syndrome as exhibited in limb levitation and groping habits in the right hand. Upon extubation scan, the results read "Consistent with cerebral infarct at the medial tips of the temporal horns, posterior frontal lobes, and towards the internal capsule". A year later, she was administered different medications; the dosages and outcomes are as follows:

- a. Baclofen treatment was tested and found to be ineffective. It showed no signs of improvement.
- b. Multiple doses of botulinum toxin (up to 300 U), which provided transient improvement of the right-hand extensors.

After 5 years, she was exposed to another round of medications. These medications seemed to work fairly well. To assess the performance and effectiveness of the medications, she was subjected to the Unified Dystonia Rating Scale to measure these im-

provements. Spontaneous limb elevations (LEs) and sudden grasps (SGs) were recorded. LEs were classified as an abrupt raising of the limb, whereas SGs were defined as any grab requiring the contralateral hand's assistance.

They are as follows

- c. She reported a dramatic decrease in the raising of the limb and virtually full halting of grabbing after two days of therapy with 1mg of clonazepam daily. When she stopped taking clonazepam, her symptoms reappeared, and when she started taking it again, she had more control over her arm. She skipped a dosage of clonazepam after four weeks of treatment. She had an episode the following day in which she grew disoriented and wielded a knife with glee. She has no memory of what happened. The electroencephalogram and MRI were normal, despite our suspicions of a seizure. The patient blamed clonazepam for the event and stopped taking it.
- d. The medial and posterior deltoid, triceps, biceps, flexor carpi ulnaris and radialis, flexor digitorum superficialis and profundus, and extensor carpi ulnaris and radialis were all treated with 600 U of botulinum toxin type A. The power and frequency of her aberrant motions were significantly reduced. Her dystonic right shoulder elevation and elbow extension also showed signs of improvement. Motor weakness was not discovered or diagnosed throughout the assessment. She said that during her follow-up treatments, her "alien gestures" were almost nonexistent.

Before therapy, she averaged 1.41 spontaneous LEs per minute and 0.82 SGs per minute. She executed an average of 0.38 impulsive LEs/min and 0.25 SGs/min after two weeks on clonazepam, a reduction of 73 % and 70 %, respectively. She completed an average of 0.23 LEs/min and 0.19 SGs/min after two sessions of botulinum toxin therapy, a decrease of 84 % and 77 % from baseline, respectively.

Case Study 4

Bakheit et al. (2013) admitted a 50-year-old man whose primary hand of use is the right hand. In

the last 24 hours before admission to the hospital, He had two generalized tonic-clonic seizures. The existence of a well-defined tumor in the right frontal parasagittal area with spread into the cingulate gyrus, as well as alterations in the periventricular white matter, were verified by an MRI head scan.

He stated that his left hand would pick up items when he did not mean to, and that once it did, it would not release them. His left hand inadvertently grabbed a person standing next to him a few times. The left hand would sometimes perform the reverse of what the right hand was doing. While he admitted that the hand was his, he claimed that it had grown a “life of its own”, and expressed astonishment and discomfort at his hand’s involuntary conduct. The patient’s ability to do bimanual activities was also harmed.

Two strategies were administered to help alleviate the effects of ALS. These therapies included maintaining mental focus on the job and intentionally diverting the affected hand to another activity (known as avoidance behavior). The latter method proved particularly effective in reducing the anarchic hand’s actions. When he was encouraged to employ this method during official occupational therapy treatment sessions, no inter-manual conflict was detected. It was however noted that mental concentration was not used in isolation as it was unable to prevent the involuntary movements.

The patient continued to employ this avoidance behavior successfully six months after his original presentation. However, his alien hand Syndrome symptoms returned when he did not use it.

Case Study 5

In a clinical AHS as reported by Demiryürek et al. (2016), a 71-year-old right-handed male patient was admitted based on suspicions of involuntary limb movements. Following the results of his clinical anamnesis and neurological evaluation, the patient was diagnosed with AHS.

An infarct in the right posterior parietal lobe was discovered via Diffusion MRI, along with a blockage in the right median cerebral artery. A blockage in the right internal carotid artery was discovered during MR angiography of the patient.

He complained of disregarding the objects in his left hand, despite the fact that he is aware of them, and that he does not always feel them. For 30-40 minutes during the day, his left hand moved involuntarily and paroxysmally, performing apparent deliberate gestures

Clonazepam 1 mg/day was started as a medicinal therapy. The patient was trained to distinguish different shapes and spatial arrangements and to apply what he had learnt to his daily tasks after being sent to the rehabilitation department for spatial recognition exercises, resulting in improved bimanual coordination and the use of a mirror box. When compared to the beginning stage, the frequency of symptoms was lower during the post-rehabilitation period. The patient continues to go to their outpatient neurology clinic on a regular basis.

Case Study 6

This is the case of a 62-year-old woman whose primary limb is right. She suffered an intracerebral hemorrhage in the left frontoparietal region. She was diagnosed with Alien Hand Syndrome in her right hand by Romano (2013) after a series of neuropsychological and standardized neurological examinations. While her movements were involuntary, she had learned to know the strange hand was hers.

She was tasked with completing an experiment that involved a Mirror box. She also completed a Visual Analogue Scale (VAS) questionnaire to assess the task’s subjective impact.

She was instructed to take a seat before a table with a box having a mirror set up for the given task. This mirror box was made out of a parasagittal mirror and an opaque box with a hole in the wall facing the patient through which she could insert her hand. In front of the mirror, the patient positioned her arms on the table with the right, injured hand within and the other outside the box. She was then asked to make a rhythmic tapping motion with her index fingers. In this case, the patient could only see the movement of her healthy hand, which created a reflection in the mirror that matched the picture of the afflicted hand, which was hidden within the mirror box. 50% of the time,

the mirror was kept open, giving visual feedback (the mirror condition), and for the other 50% of the time, it was closed, giving no visual feedback.

For a total of 16 blocks, each condition was shown 8 times in a counterbalanced sequence. The amount of tapping motions produced by the alien hand in 15 seconds was tallied to see if there was any positive change in the patient's motor control. The theory is that seeing a mirror reflection that matches the picture of the afflicted hand improves motor control, which increases the recurrence with which the affected hand taps.

The results showed a fine improvement in both the quantitative and qualitative movements of the alien limb in the sessions where she was allowed to see her normal hand in the mirror as opposed to the sessions where she was not allowed to see her normal hand in the reflection. However, it is worth noting that this therapy was performed under strict experimental conditions just once due to clinical limitations present within the clinical facility. During a 5-day rehabilitation exercise, she performed this therapy and noticed stable improvements although the symptoms persisted, but in lower frequencies.

LIMITATIONS/CHALLENGES

A careful evaluation of all case studies presented in this review revealed several challenges and limitations. These were shared commonly in all cases. The complexity in diagnosis poses challenges from diagnosis to rehabilitation and after-care. Some of these limitations/challenges are discussed below

- a. Generalizability: it is difficult to extrapolate the results to other instances due to the distinctive nature of each Alien Limb Syndrome case, which demands a personalized strategy. This is time and resource-extensive.
- b. Diagnostic complexity: because Alien Limb Syndrome is rare and subjective, diagnosing it can be difficult and may lead to diagnostic doubt.
- c. The multidisciplinary approach to rehabilitation means that in every case different personnel across different specialties are expected to

be actively involved in the proper diagnosis and treatment. Getting the different personnel together at the right time poses a huge challenge for effective and timely treatment.

- d. In motor impairment cases, getting patients into appropriate therapeutic activities helps to enhance their functional results. Consequently, the difficulty is in offering treatment in sufficient amount and intensity, particularly for the hand and upper limb

EMERGING TECHNOLOGIES IN ALS REHABILITATION

Technology is a major driver in improving rehabilitation techniques and success in cases with motor impairments. In one of the cases cited above, mirror-box therapy was used to increase the chances of full recovery. While this is an archaic method, new technologies have improved this system.

Numerous technical strategies have been put forth to support this. One such technology is virtual reality (VR), which has shown promise in improving motor function during stroke therapy (Laver et al., 2015). Additionally, using VR might lead to a higher treatment intensity, which would benefit patients even more. VR systems are categorized into two primary groups. The first is mechanical or robotic systems, where virtual reality is just employed as an accessory to facilitate the performance of motions (Sampson et al., 2012). The second kind of case involves VR offering a significant therapeutic intervention on its own. This could take one of two forms:

an ecologically valid simulation of a daily task or tasks, with the ability to dynamically adjust the task's difficulty based on the patient's performance.

the provision of visual signals to stimulate neural activity and potentially activate brain adaptation processes to aid in the recovery of stroke-related impairments.

Augmented Reflection Technology (ART), a form of Virtual Reality, was conceptualized and developed based on the principles of Mirror Therapy (Regenbrecht et al., 2014). All the features

of conventional Mirror Therapy are included in ART, along with additional computer-mediated visual illusions and workout options. It has been demonstrated, in particular, that the ART's "fooling" capacity outperforms the Mirror Box by up to three times. Participants are more frequently duped into thinking that the mirrored hand on one side of the screen is that side's hand when, in reality, it is the other hand (Regenbrecht et al., 2014). By measuring the frequency and intensity of referred sensations generated by the mirror visual illusion, ART also enabled the user to create a strong sense of ownership of the exhibited limb (Hoermann et al., 2012).

CONCLUSION

Alien Limb Syndrome (ALS) is an uncommon neuropsychological condition in which patients report uncontrollable and unintentional motions of the affected limb (Schaefer et al., 2016). Since the first recorded case of Alien Hand Syndrome in 1908, scientists have found it difficult to understand the precise underlying mechanisms of its pathology. Furthermore, they have been unable to establish an accepted mode of therapy and rehabilitation for patients.

Numerous cases of AHS have been treated with a variety of methods ranging from pharmaceutical therapy to rehabilitation therapy. The most successful among the cases highlighted in this article is the therapy administered by Pappalardo (2004), where the patient was examined 24 months after rehabilitation and there were no signs of involuntary movement or intermanual conflict. Drugs have also been used as a therapeutic means to bring the patient back to full control of one's hand. Drugs such as Clonazepam at 1 mg/day and 600 U of botulinum toxin type A been proven to alleviate the frequency and effect of ALS, however, there has been no report of a 100% success rate using drugs such as Clonazepam at 1 mg/day and 600 U of botulinum toxin type A.

With many unanswered questions and the evolution of the understanding of the somatosensory and motor pathways, scientists are working on new and better ways to completely restore full control and functionality to the alien hand.

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