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# Alien hand syndrome

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Alien limb phenomenon; Anarchic hand; Diagnostic dyspraxia; Groping-grasping reaction; Intermanual conflict; Magnetic apraxia; Strangelovian hand; Unilateral apraxia; Wayward hand

## Historical note and nomenclature

Alien hand syndrome is not consistently or precisely defined. It describes complex, goal-directed activity in one hand that is not voluntarily initiated. The patient is unable to explain the source of such movement and may consider the limb to move as if it had a mind of its own.

Essentially, two kinds of behavior are covered by this term (Feinberg et al 1992). The first consists of repetitive involuntary grasping. Beginning in 1900, Liepmann drew attention to the unilateral, disinhibited grasp reflex to tactile stimulation after cerebral injury (Liepmann 1905), although this phenomenon had been described by Kaiser as early as 1897 (Schuster 1923). Liepmann's detailed descriptions of disinhibited grasp reflex and unilateral apraxia quickly inspired other German investigators to contribute their own observations of acquired complex movement disorders. Among them, Van Vleuten reported a patient with a left hemisphere brain tumor that had invaded the corpus callosum (Van Vleuten 1907). The patient repeatedly grasped and put down an object with his right hand, apparently unintentionally. Goldstein first connoted the "alien" quality of unilateral repetitive grasping, the impression that an alternate entity is responsible for the behavior (Goldstein 1908). His patient complained, "There must be an evil spirit in the hand!" In succeeding years, such behavior became formally labeled by terms that included, "pseudospontaneous movements" (Wilson and Walshe 1914), *Nachgreifen* ("after-grasping") (Schuster 1923), "magnetic apraxia" (Denny-Brown 1958), “manual grasping behavior” (Lhermitte 1983), the "groping-grasping reaction" (Magnani et al 1987) and “visual groping” (Yagiuchi et al 1987).

The second behavior covered by the term “alien hand syndrome” involves unilateral goal-directed limb movements that are contrary to the individual's intention and not accounted for by repetitious grasping or unilateral apraxia. Van Vleuten's patient appears to have been the earliest reported instance of this condition (Van Vleuten 1907). In this case, the patient's left hand was not only apraxic, but also performed markedly incorrect actions, such as touching his right hand instead of his nose, despite his understanding the command, and failing to move when commanded. Self-oppositional behavior, wherein one limb counteracts the declared or consciously intended action of the other limb, was often noted after complete or partial surgical division of the corpus callosum (callosotomy) to treat refractory epilepsy (Van Wagenen and Herren 1940; Smith and Akelaitis 1942). Akelaitis termed such behavior "diagnostic dyspraxia" (Akelaitis 1945).

Brion and Jedynak coined the term *la main étrangère* (the foreign hand) to describe diverse behaviors in patients with callosal tumors that included either the failure to recognize self-ownership of the limb or the absence of self-control over the limb's goal-directed actions (Brion and Jedynak 1972). In either case, the disturbance conveyed the impression of an alternative, silent, simultaneously coexisting "self" governing one side of the body, contrary to the bodily awareness and control that could be accessed introspectively. Of these 2 disturbances, the former is better termed “somatoparaphrenia” (Joynt and Goldstein 1975) or “asomatognosia” (Thomas et al 1998) and is usually associated with hemianesthesia.

Self-oppositional activity was also termed "intermanual conflict" by Bogen (Bogen 1979); he introduced the English term "alien hand," a translation of Brion and Jedynak's *la main étrangère*. Bogen intended "alien hand" to indicate a milder state of intermanual conflict among patients with surgical callosal lesions, wherein the individual finds one hand strange or uncooperative. Goldberg and colleagues applied this term to stroke patients with intermanual conflict, one of whom also had disinhibited groping (Goldberg et al 1981). From this point onward, "alien hand" came to describe these 2 different motor disorders: (1) disinhibited groping and (2) self-opposition. However, investigators have not exercised restraint when reporting involuntary movements or postures in their patients. Thus, "alien hand" has been extended to include nongoal-directed, involuntary tonic posturing (Bundick and Spinella 2000; Inzelberg et al 2000), even though the patient may not indicate any sort of alien quality (Ball et al 1993). Nonspecific epileptic movements that are associated with feelings of loss of ownership for the limb have also been reported as “alien limb” (Boesebeck and Ebner 2004). These unfortunate corruptions of the term complicate its usefulness.

Della Sala and colleagues proposed "anarchic hand" as an alternative term for self-conflicting limb activity (Della Sala et al 1991), because afflicted patients do not consider the limb itself to be alien and also to provide a more strict definition than that intended by "alien hand." Nonetheless, "alien hand" appears to have become the preferred term for these disparate disturbances of motor self control. This is regrettable because different pathophysiological mechanisms probably underlie the diverse behaviors in alien hand. Considering the wide variety of acquired disorders of voluntary movement, what constitutes or does not constitute alien hand seems to have been arbitrarily decided.

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## Clinical manifestations

Alien hand syndrome is an intermittent involuntary movement disorder. The patient must be aware of the disturbance (at least some of the time) to indicate the lack of voluntary initiation of the abnormal activity. The movement must appear to be directed to a particular object or to conduct a specific task. Nonspecific involuntary muscular contractions (eg, clonus, tremor) are, therefore, excluded. The patient's comments should convey the impression that the involved limb behaves as if it were under the purposeful command of an individual other than the patient. Such comments may reflect depersonalization so that the errant hand assumes a distinctly different "personality." The patient may complain of the hand, "It doesn't want to stop," or, "I can't make it listen to me." Autocriticism is not unusual; patients may criticize or even slap the "alien" hand with the "good" hand (Leiguarda et al 1989; Della Sala et al 1994; Chan et al 1996). Alternatively, patients may regard the autonomous hand affectionately (Della Sala et al 1994; Groom et al 1999) or with amusement (Pack et al 2002). One case report documented both positive and negative attitudes toward the hand (Lewis et al 1997). Patients usually recognize that they have an illness that induces the

disturbance, rather than believe that a supernatural force possesses them. Nonetheless, the involuntary activity may incite not just anger and frustration but fear of self-harm (Levine and Rinn 1986; Leiguarda et al 1993); patients' comments may suggest control by an evil entity (Goldstein 1908; Leiguarda et al 1993). Patients generally do not believe that they have a psychiatric disorder responsible for the disturbance. At times, patients may be either unaware of, or may deny, their involuntary goal-directed actions (Leiguarda et al 1989).

Three kinds of alien hand are now recognized. In the first, termed “the frontal variant”, the patient has disinhibited groping, an unintended reaching out toward visible objects that fall within arm's reach (visual grasp) or that have been removed from contact with the hand. Self-directed grasping may also occur, which may even awaken the person from sleep (Banks et al 1989; Nicholas et al 1998; Ortega-Albas et al 2003; Giovannetti et al 2005). Once seized, the patient has difficulty letting go of the object and may repeatedly clutch at the object when holding it. The behavior may even involve involuntary sexual self- or other-person-fondling that may publicly embarrass the patient (Della Sala et al 1991; Gasquoine 1993a; Ong Hai and Odderson 2000). Paradoxically, the patient may have difficulty willing the limb to move. Patients sometimes describe an urge to move in this variant (Chan and Liu 1999). The grasp reflex to tactile stimulation is usually present, although some exceptions have been reported (Gasquoine 1993a; Marchetti and Della Sala 1997), and tone is increased in the limb. A tightening of the grip occurs the more that the patient attempts to release the object. With concentrated effort the patient can release the object; however, with distraction the phenomenon may be reinstated (Walshe and Robertson 1933). Anxiety may aggravate the behavior (Gasquoine 1993a). In one remarkable case, the patient's excessive grasp could only be alleviated (reliably) by command from another individual (Kritikos et al 2005). An associated finding may be reduced speech output with intact comprehension and repetition, or transcortical motor aphasia, if the lesion involves the left medial frontal cortex (Gasquoine 1993a; Tow and Chua 1998). The right hand is more often involved than the left hand, reflecting the greater association with left hemisphere injury (Feinberg 1997).

In the second kind of alien hand, termed “the callosal variant,” the patient's hand counteracts voluntary actions performed by the other "good" hand. For example, the patient may pull off a sock immediately after it has been put on, close a drawer that has just been opened, turn a car's steering wheel in the opposite direction of that of the good hand, etc. (Barbeau et al 2004). In general, such self-oppositional behavior does not appear unprompted but rather follows an action voluntarily produced by the unaffected limb. This is termed “intermanual conflict” and is distinguished from behaviors wherein the alien hand interferes with activity by the good hand without “undoing” the good hand's action (Chan and Ross 1997). Sometimes the alien behavior seems not to counteract the unaffected limb's activity but instead acts without a clear functional relationship to the action of the unaffected limb (Tanaka et al 1996). Occasionally, the involuntary movement occurs without being preceded by activity in the unaffected limb (Gottlieb et al 1992). The alien behavior may occur without the patient immediately being aware of it, and an urge to move has not been reported when this variant occurs without frontal alien hand concurrently (Chan and Liu 1999). Another phenomenon associated with callosal alien hand has been termed agonistic dyspraxia, in which one hand does not respond to command and the contralateral hand compulsively performs the requested act (Lavados et al 2002). Following callosal injury, either hand may behave in this manner. Callosal alien hand nearly always affects the left hand (Feinberg 1997), but at least one instance has been reported where the dominant right hand apparently acted in

this manner - that is, at least showed intermanual conflict (Giovannetti et al 2005). The grasp reflex and increased muscular tone do not always occur (Suwanwela and Leelacheavasit 2002). The disorder may be more frequent when the patient is fatigued (Baynes et al 1997), stressed (Goldberg and Bloom 1990; Della Sala et al 1994; Cantagallo and Boldrini 1997; Kikkert et al 2006), or required to divide attention between concurrent activities (Giovannetti et al 2005).

Less commonly, a third kind of alien hand has been reported, consisting of ataxic limb movements associated with anesthesia or hypesthesia of the limb (Levine and Rinn 1986; Dolado et al 1995; Ventura et al 1995; Ay et al 1998; Groom et al 1999; Bundick and Spinella 2000). This has been termed “the sensory alien hand variant” (Ay et al 1998). The limb anesthesia prevents proprioceptive monitoring of limb position, and this in turn may impair motor control of the limb as well as hinder recognizing the limb as part of one's own body. An epileptic variety of this has been reported (Feinberg et al 1998). Marey-Lopez and colleagues described a patient with sensory alien hand variant who had hemianesthesia associated with arm levitation, but with also compulsive groping similar to the frontal variant (Marey-Lopez et al 2002). Furthermore, their patient denied self-ownership of the limb when she touched it without visual guidance, consistent with Brion and Jedynak's seminal *la main étrangère* case reports (Brion and Jedynak 1972). The patient reported by Marey-Lopez and colleagues had a right thalamic infarction. Similar findings were reported to also follow occipital infarction (Lewis et al 1997) and parietal infarction (Marti-Fabregas et al 2000).

A similar disorder has been observed following acute parietal injury but without evident tactile impairment. It consists of involuntary limb posturing and exploratory movements, unilateral neglect, and denial of the disorder (Horenstein et al 1988). This disorder may arise due to loss of parietal input to motor cortex, causing impaired voluntary movement regulation by motor cortex that may be exacerbated by inattention to the limb. This third variant may not so convincingly be regarded as alien hand as the other two, because the movements lack a clearly purposeful character.

Alien hand generally follows acute focal cerebral injury, most commonly cerebral hemispheric stroke or corpus callosal surgery to treat epilepsy. It also appears in a variety of degenerative, dementing cerebral disorders. Hence, a variety of coexisting symptoms and signs appear, depending on the localization and pathology. Alien hand associated with medial frontal injury may be accompanied by lack of initiative, transcortical motor aphasia, and other signs that characterize medial frontal injury (Chamorro et al 1997). In contrast, alien hand that follows callosal disruption may be associated with signs typical of interhemispheric disconnection; there may be dominant hand constructional apraxia, nondominant hand ideomotor apraxia, apraxic agraphia, tactile anomia, and inability of one hand to imitate the posture of the opposite hand or to find an object palpated by the opposite hand with the eyes closed (Bogen 1993). Alien hand that occurs with posterior cerebral injury is associated with anesthesia of the limb and sometimes ataxic movements of the hand and visual field deficit (Levine and Rinn 1986; Ay et al 1998; Groom et al 1999). Alien hand that occurs in degenerative, dementing illnesses such as cortical-basal ganglionic degeneration and Alzheimer disease is usually accompanied by ideomotor apraxia and rigidity of the limb, along with other disturbances characteristic of the particular disorder (eg, aphasia, confusion, memory loss, oculomotor paresis, etc.) (Riley et al 1990; Green et al 1995).

Involuntary oppositional behavior of one leg may also appear, often ipsilateral to the alien hand (Van Vleuten 1907; Akelaitis 1945; Bogen 1993; Della Sala et al 1994; Markus et al 1995; Rediess and Satran 1995; Chan et al 1996).

Often, the two most common kinds of alien hand appear in the same individual (Goldberg et al 1981; Goldberg and Bloom 1990; Gasquoine 1993b; Nagumo and Yamadori 1995; Chan et al 1996; Giovannetti et al 2005), including one kind of alien hand in one limb and the other kind of alien hand in the other limb (Van Vleuten 1907; Cantagallo and Boldrini 1997). Alternatively, the same kind of alien hand (either self-oppositional behavior or involuntary grasping) may appear in both upper extremities (Leiguarda et al 1989; Mark et al 1991; Gasquoine 1993a; Calmus et al 2005).

A few case reports have indicated self-contradictory communicative behavior (gestures or speech) in patients following callosal damage (Akelaitis 1945; Gazzaniga 1970; Poncet et al 1978; Mark 1990; Hendry and Holliday 1996; Plas et al 1999; Lausberg et al 2000; Nishikawa et al 2001). This indicates that self-oppositional behavior is not limited to limb motor disturbance. Gasquoine reported a patient with frontal alien hand who involuntarily expressed his thoughts, but the report did not indicate whether the content was alien to intent (Gasquoine 1993a).

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## Clinical vignette

A 71-year-old right-handed woman developed acute left hemiparesis and visual hallucinations. She also complained that her left hand uncontrollably scratched her and pulled at her hair. Past medical history was notable for chronic hypertension and triple coronary artery bypass graft 6 years earlier. Two weeks before the illness, she had felt diffusely weak; another hospital had attributed this weakness to metoprolol toxicity. When her complaints did not subside after 2 days off medication, her husband brought her to the emergency room. Evaluation disclosed full orientation, left lower facial weakness, right gaze bias, left hemibody hypesthesia, and extensor posturing of the left limbs, with the left hand constantly clenched. Cranial CT scan indicated acute right parietal cortical infarct and extensive bilateral subcortical white matter ischemic changes.

She was hospitalized and experienced no further hallucinations. She initially had constructional apraxia and impaired temporal orientation and abstraction. Her Mini-Mental State Exam score (Folstein and Folstein 1975) improved from 18 to 23 (maximum score is 30) during her stay. Cerebral MRI scan 6 days after admission confirmed the subacute right parietal infarct and diffuse bilateral subcortical ischemic changes. Carotid ultrasound examination indicated no surgically significant disease, so she was transferred to a rehabilitation hospital 9 days after admission. On the patient's arrival, the physician wrote in her chart, "The patient refused to attempt to do anything with that hand because 'it will hit me in the face.' The patient talks of her hand as if it were a separate entity."

Self-care ability improved during the 1-month rehabilitation stay but was nonetheless disrupted by the left hand's involuntary grasping and failing to release objects despite being commanded to do so. However, "the patient could actively request the hand verbally to let go of objects, and this sometimes resulted in improved control. The patient also demonstrated an increasing ability to spontaneously use the left upper extremity when not having conscious effort directed towards that function."

Informal follow-up evaluation in the patient's home about 10 weeks after illness onset disclosed consistent involuntary left hand grasp to gentle tactile stimulation and a tendency for the left hand to repeatedly touch her face with her eyes closed, despite being instructed to keep the upper extremities extended. She also showed bilateral tactile anomia, agraphesthesia, and impaired joint position sense. Light touch sensitivity was symmetrically present in the upper extremities. The left arm showed tonic posturing; it would either be

maintained at rest with the elbow flexed or was pronated when the arms were outstretched. The right arm moved normally. No autonomous groping was observed. Further information on the patient's outpatient course is not available; she died within the year.

**Discussion.** Alien hand was suggested by the patient's involuntary self-grabbing and her referring to her hand in depersonalized terms. The etiology was somewhat unusual because the apparently acute radiologic finding was a contralateral parietal infarct. However, the neuroimaging studies suggested chronic paracallosal ischemic leukoencephalopathy. Possibly the combination of left hypesthesia induced by the acute parietal infarct with chronic medial frontal ischemia sufficed to induce alien hand. Thus, the patient showed poor awareness for the spatial location of the arm, and this in turn may have impaired somatosensory feedback that would otherwise have prevented her left upper extremity from groping at her face due to medial frontal injury. The medial ischemic damage alone may have been insufficient to cause alien hand. Thus, the patient may have had the sensory alien hand variant (Ay et al 1998). Unfortunately, other case reports with similar clinical and radiologic presentations have not appeared for comparison.

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## Localization

Various kinds of alien hand are associated with different locations of structural damage. The disorder characterized by groping is usually associated with damage to the contralateral medial frontal cortex, near or involving the supplementary motor area (Goldberg et al 1981). The lesion is contralateral to the affected hand and is 3 times as likely to be in the left hemisphere than in the right (Feinberg 1997). Self-oppositional behavior is associated with damage to the body of the corpus callosum, particularly the ventral portion of the posterior third of the callosum (Tanaka et al 1996). Often, however, these 2 variants of alien hand are found together, and structural damage involves both the medial frontal cortex and the corpus callosum.

A third, less commonly reported location for injury associated with alien hand is in the posterior cerebral cortex or underlying structures (Levine and Rinn 1986; Ventura et al 1995; Ay et al 1998; Groom et al 1999; Bundick and Spinella 2000; Marey-Lopez et al 2002). Two patients have been reported with ictal alien hand following contralateral parietal injury (Leiguarda et al 1993). One patient suddenly felt uncertain about the arm's spatial location, whereas the other patient suddenly sensed that the arm did not belong to her. Another report of ictal alien hand with similar features followed from frontotemporal lobe lesion (Feinberg et al 1998). Three patients have been reported with acute parietal injury, without clinically evident somatosensory loss, but with hemibody neglect and denial of their autonomous limb movements (Horenstein et al 1988).

Alien hand also has been frequently associated with cortical-basal ganglionic degeneration. In such patients, the achromasic, ballooned neurons and neuronal loss occur primarily in the frontal and parietal lobes, thalamus, and substantia nigra (Gibb et al 1990; Riley et al 1990).

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## Pathophysiology

The variants of alien hand differ not only in character but also in localization. Disinhibited groping that occurs consistently with tactile or visual stimulation is primarily related to medial frontal lobe injury, whereas self-oppositional behavior occurs more variably in the patient and is primarily associated with mid-callosal damage (Tanaka et al 1996). Alien hand associated with impaired somatosensory

input usually follows posterior cerebral injury. Therefore, different pathophysiologic mechanisms are likely responsible. The feeling of alienation likely results from the combination of disinhibited, excessively reactive responses that appear to be purposeful, perceived by an individual with intact error monitoring (Biran et al 2006).

The frontal variant of alien hand may reflect disinhibited parietal function. Denny-Brown demonstrated during his experimental work in monkeys and observations on humans with localized lesions that the frontal and parietal lobes seem to have reciprocal functions (Denny-Brown 1956). Parietal injury results in inattention and lack of orientation toward contralateral space, or unilateral neglect syndrome. In rare cases of parietal injury, the patient may extend rather than flex the fingers to the approach of a stimulus; Denny-Brown termed this “avoidant reaction.” In contrast, frontal injury, particularly in the supplementary motor area of the medial frontal lobe, results in contralateral disinhibited grasp reflex and groping. From these observations, Denny-Brown concluded that the individual's relationship to surrounding space involves a balance between approach and avoidance. The frontal lobes are specialized for avoidance, whereas the parietal lobes are specialized for exploration. Frontal lesion may result in disinhibited exploration (groping), whereas parietal lesion may result in excessive environmental withdrawal, avoidance, or unawareness. Observations in one case study following medial frontal injury indicated that erroneous object grasping were related to the proximity of the objects to the alien hand (Giovannetti et al 2005).

Goldberg and Bloom revised Denny-Brown's ideas to suggest that the medial frontal cortex is part of a medial premotor system that anticipates movement and, thus, is vital for monitoring internally-generated voluntary control. In contrast, a separate, lateral premotor system primarily reacts to external stimuli. Hence, medial frontal damage interferes with the patient developing a sense of purpose to movement generated by the reactive lateral premotor system under parietal disinhibition, resulting in alienation (Goldberg and Bloom 1990). Environmental stimuli may not only stimulate particular motor patterns, but also be used to cue correct performance. Therefore, patients with movement disorders following either medial frontal injury (such as alien hand) or medial frontal hypometabolism (such as parkinsonism) may benefit when they are cued to attend to their motor performance (Oliveira et al 1997).

The frontal alien hand variant may occur in either hand and reflects contralateral medial frontal injury (Leiguarda et al 1989). However, the frontal variant more commonly affects the dominant hand (Feinberg et al 1992), perhaps because right (nondominant) hemispheric injury is more likely to produce hypokinesia of the contralateral hand than is left (dominant) hemispheric injury. Such hypokinesia may overshadow alien hand resulting from right hemispheric injury (Chan and Ross 1997).

The callosal alien hand variant occurs preponderantly in the nondominant hand (Feinberg et al 1992; Chan and Ross 1997). This asymmetry may arise because voluntary, particularly skillful activity is primarily mediated by the left cerebral hemisphere (Heilman and Rothi 1993), at least among right-handed individuals. The callosal pattern may emerge from the left hemisphere's failure to inhibit the right hemisphere through the corpus callosum (Feinberg et al 1992). Tanaka and colleagues proposed that callosal injury blocks communication between the superior parietal lobule of each hemisphere (Tanaka et al 1996). The desire for a specific movement may occur in both hemispheres simultaneously. Without the communication between the left and the right superior parietal lobules, each hemisphere may independently prepare to conduct the desired action with the contralateral hand, leading to self-conflict. The left hemisphere's lack of influence

on the right after callosal injury is variable, for unknown reasons, leading to intermittent alien hand alternating with cooperation between the hands. However, this hypothesis does not explain why the callosal alien hand may reverse the dominant hand's action (such as closing a drawer when the dominant hand has opened it), rather than merely compete to control an object. Such reversal suggests that the right hemisphere may evaluate the right (dominant) hand's action that is not under its control, and react by the left hand's reversal of the action, because the right hand's action does not match the right hemisphere's intent. This could explain the repeated cycling of alternating and opposing hand control that has been described for some common activities among split-brain patients (Akelaitis 1945).

The sensory alien hand variant, caused by predominantly posterior cerebral injury, may arise from the combination of contralateral hemianesthesia and ataxic limb movements (Levine and Rinn 1986; Dolado et al 1995; Ay et al 1998). The dense sensory loss of the limb may interfere with the individual's recognition of self-ownership and, hence, the patient may attribute spontaneous limb movements (that occur without proprioceptive feedback and thus may be clumsy and dissociated from conscious intent) to the activity of an independent entity.

Horenstein and colleagues reported 3 parietal-lesioned patients without alien hand (due to their failure to acknowledge the deficit) who had clinically intact tactile function but involuntary posturing of the contralateral limb and contralateral neglect (Horenstein et al 1988). One of the patients appeared to have exploratory finger movements that compromised self-care. The authors suggested that despite the lack of clinically evident somatosensory dysfunction, the disturbance arose from interference with parietal afferents to ipsilateral primary motor cortex, thus leading to impaired regulation of voluntary movements, exacerbated by spatial neglect. They termed the disorder "strangelovian hand" after the protagonist in the 1964 Stanley Kubrick movie "Dr. Strangelove," whose crippled right arm showed involuntary self-aggression and fascist salutes. The same sobriquet has been applied by other authors to alien hand (Gasquoine 1993a; Della Sala et al 1994).

Often, lesions in acquired cerebral disorders are not restricted to one lobe, the callosum, or one side of the brain. The foregoing mechanisms may interact to produce diverse manifestations of alien hand within the same individual.

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## Differential diagnosis

A wide variety of disorders may be associated with involuntary movements that superficially resemble alien hand. The diagnostic features of alien hand alone are broad, including 3 distinct disorders. Thus, the diagnostic criteria for alien hand seem arbitrary, partly because certain other similar disturbances are not usually included. Nonetheless, familiarity with the differential diagnosis of alien hand not only facilitates diagnosis and treatment but also invites considering the physiologic basis for willed movements.

The disinhibited grasp reflex is often seen in alien hand syndrome, but it is also a common feature of either focal cerebral injury (De Renzi and Barbieri 1992) or degenerative dementing cerebral disorders without alien hand (Vreeling et al 1995) and normally occurs in infancy. The grasp reflex by itself (ie, without groping or self-opposition) should not be considered alien hand, because the disturbance is comparatively simple and is less likely to disrupt patient activities. In such cases the patient does not regard the hand as an independent entity.

Dystonia often has a unilateral presentation. Hemiballism (Dewey and Jankovic 1989), unilateral intention tremor, parkinsonism (Blonder et al 1989; Tison et al 1993), chorea (Dilenge et al 1997), and asterixis (Massey et al 1979) are not

unusual. They differ from alien hand by not involving goal-directed movements in themselves, although dystonic movements may increase during any kind of willful limb movement.

Unilateral spontaneous arm levitation is often an aspect of alien hand that is seen in cortical-basal ganglionic degeneration. However, unilateral spontaneous arm levitation may also appear in progressive supranuclear palsy; therefore, distinguishing between these illnesses may be difficult (Barclay et al 1999). Spontaneous arm levitation does not in itself constitute alien hand, because no apparent goal-directed behavior is evident. Cases in which spontaneous arm levitation is associated with denial of limb ownership have been termed alien hand (Carrilho et al 2001) but appear to represent variants of somatoparaphrenia instead. Progressive supranuclear palsy is not associated with alien hand (Litvan et al 1997). Cortical-basal ganglionic degeneration may be distinguished from progressive supranuclear palsy by stimulus-sensitive myoclonus and somatosensory loss, whereas progressive supranuclear palsy characteristically restricts vertical eye movements and is associated with backwards falling.

Focal motor seizures do not involve goal-directed behavior. However, paroxysmal alien hand due to presumed seizures has been described in several patients (Leiguarda et al 1993; Rubboli et al 1998). Cortical reflex myoclonus, a kind of paroxysmal dyskinesia, is similarly without intrinsic goal-directed behavior but may be provoked by voluntary movement (Hallett et al 1979). This disorder has been observed in some patients with alien hand (Van Vleuten 1907; Ball et al 1993; MacGowan et al 1997).

Action tremor is commonly encountered following posterior cranial fossa injury. This is usually a goal-directed disorder (for example, seen on finger-to-nose pointing), but the patient's acknowledged desire to reach for a specific target distinguishes this disturbance from alien hand.

Psychogenic dystonia should also be considered. Its features are variable presentation, often accompanied by pain, "give-away" weakness, responsiveness to psychotherapy, suggestion, or placebo, and occurrence with multiple somatizations or "obvious" psychiatric disturbance (Lang 1995). In contrast, alien hand is generally not associated with psychiatric disorder and is not provoked by suggestion. Nonetheless, alien hand may be mistaken for a psychiatric disorder (Van Vleuten 1907; Akelaitis 1945), particularly if clinicians are unfamiliar with the presentation.

Synkineses are unintended movements that accompany simple voluntary movements, but rather than appearing as the self-interfering movements typical of alien hand, they either mimic the voluntary movement or involve tonic posturing. Bimanual synkineses (Schott and Wyke 1977; Trouillas et al 1990) are upper extremity movements that crudely imitate the contralateral limb. More accurate imitations may be termed “mirror movements” (Haerer and Currier 1966). A wide variety of acquired and congenital disorders may be responsible, including the Klippel-Feil syndrome (Farmer et al 1990) and Kallmann syndrome (Zlotogora 1995). Mirror movements may also occur commonly following stroke (Nelles et al 1998). Bimanual synkineses are also a normal developmental finding in childhood. In this vein, sometimes mirror writing is also considered (an unintended reversal of individual letter or ideogram formation) (Chia and Kinsbourne 1987). Mirror movements may occur in alien hand syndrome, but alien hand syndrome is distinguished by including more complex movements as well (Gottlieb et al 1992).

Associated movements of hemiplegia (Walshe 1923; Blin et al 1994) are a kind of synkinesis wherein the plegic limb adopts nonspecific increased tone (shoulder

abduction, elbow flexion, and finger extension) during yawning or stretching of the unaffected limb. These movements commonly occur in stroke.

Complex movements may occur during pathologically altered arousal or personality disorders, such as REM sleep behavior disorder (Schenck et al 1993), sleepwalking, sleep-related eating disorder (Schenck et al 1991), partial complex seizure disorder, and dissociative personality disorder (including multiple personality disorder) (Task Force on DSM-IV 1994; Cantagallo et al 1999). These are similar to alien hand by being involuntary and goal-directed. However, patients with alien hand are alert and attentive when the disorder occurs and can usually comment on the behavior. In contrast, the movement disturbances that occur with alterations of arousal or personality are not recalled by the individual or "core personality." There should be no mistaking the rare occurrences of self-conflicting communicative behavior following corpus callosum injury (Mark 1990) with dissociative personality disorder (Cantagallo et al 1999).

Delusional and attentional disturbances should be considered. Complete anesthesia or deafferentation of a limb may cause denial of its ownership (Sacks 1984; Brown 1989), a form of somatoparaphrenia (Joynt and Goldstein 1975) or asomatognosia (Thomas et al 1998). This disturbance was called *la main étrangère* by Brion and Jedynak (Brion and Jedynak 1972), from which the term "alien hand" was derived, but alien hand is now recognized as a disturbance of voluntary movement origination rather than impaired self-recognition. Motor impersistence (Joynt and Goldstein 1975) is similar to alien hand in that there is a failure of voluntary control, as voluntary control is thought to have an attentional basis. However, alien hand does not involve a failure to sustain muscle contraction once it has started but, rather, involves failure to initiate limb movement (contrary to one's intention) or to restrain unintended activity. Motor neglect (Critchley 1953; Laplane and Degos 1983; Chamorro et al 1997) appears similar to alien hand in that the patient fails to move a limb under certain circumstances. However, in alien hand the limb may fail to move when the patient is so commanded, and this is the opposite for motor neglect.

Patients with frontal injury may show impaired impulse control (Stuss and Benson 1986), particularly following orbitomedial injury (Truelle et al 1995). Such behavior reflects the failure to withhold a response to a certain stimulus, usually visual. Impaired impulse control applies to actions involving the entire body rather than being isolated to one limb as in alien hand. Specific subtypes of impaired impulse control include utilization behavior (Lhermitte 1983), imitation behavior (De Renzi et al 1996), and the environmental dependency syndrome (Lhermitte 1986). However, a variant of utilization behavior has been reported that is termed “compulsive manipulation of tools” (Mori and Yamadori 1982; Motomura et al 1988), wherein primarily one hand uses tools impulsively although the other hand restrains it. This appears indistinguishable from alien hand.

Another disturbance of disinhibited response is continuous perseveration, wherein the patient produces an activity (eg, drawing loops) or verbal expression that was initially appropriate but is then automatically repeated needlessly, as if the action itself prompts reproduction. This has been primarily associated with right hemisphere injury (Sandson and Albert 1987), although one patient with unwanted unilateral continuous motor perseveration had a left pericallosal infarct (Shahani et al 1970). Patients with alien hand may show response perseveration, but alien hand generally is not continuously perseverative, whereas continuous perseveration enlists the production of an initially voluntary response, unlike alien hand.

Similar to continuous perseveration is facilitory paratonia (Beversdorf and Heilman 1998), wherein the patient actively, yet involuntarily, continues an

alternating limb movement that was initially passively conducted by the examiner. The phenomenon can cease with verbal command, yet patients for some reason do not stop on their own, despite realizing that the movement is peculiar. They do not regard the phenomenon as alien (Kral 1949). The disorder reflects frontal lobe dysfunction.

Unilateral ideomotor apraxia is almost invariably present in the callosal alien hand variant and may also be seen in patients with visual grasp (Geschwind and Kaplan 1962), but it may occur without alien hand (Ceccaldi et al 1995). Unilateral ideomotor apraxia results in unintended abnormal hand postures and movements, and the patient is usually aware of being incorrect and strives to improve performance, albeit unsuccessfully. The patient voluntarily initiates the movements, with no inherent self-opposition or disinhibited groping, thus distinguishing unilateral apraxia from alien hand. Patients with apraxia may commit “content errors,” wherein they produce skillful movements that are thoroughly inappropriate to the task (De Renzi and Lucchelli 1988; Rothi et al 1988; Ochipa et al 1989; 1992). Although superficially similar to callosal alien hand, these reports have not indicated any self-critical or self-corrective behavior as is found in alien hand, thus suggesting that the patients were impaired in tool use concepts instead.

In the graphic disconnection syndrome, patients with severe aphasia and right hemiparesis may show aphasic agraphia with the left hand, whereas their right hand, when assisted with a writing prosthesis, may show improved spelling and more appropriate word writing but clumsy execution (Brown et al 1983; Leischner 1983; Friedland 1990; Lorch 1995). The left hand productions are presumed involuntary, because the responses are either spelled incorrectly or incorrect words are produced, unlike those of the right hand. The act of writing itself is not involuntary and, therefore, the disorder is not alien hand, but it is similar to self-contradictory communicative behavior that may appear after callosal injury (Mark 1990), in that the individual's accuracy of expression appears to depend on the hemisphere that is primarily engaged at the moment.

Tics are brief, contextually inappropriate movements and, thus, are not readily confused with the more prolonged and complex movements of alien hand. Nonetheless, a case report of "signing tics" in Tourette syndrome (Lang et al 1993) showed that fingerspelling and semantic hand gestures could become incorporated in the disorder. Tourette syndrome is characteristically associated with obsessive-compulsive symptoms. Obsessive-compulsive disorder itself may include inappropriate motor activity, such as excessive cleaning or hair pulling. Nonetheless, in tics (and perhaps compulsions) the patient feels an "urge" to conduct the inappropriate behavior "intentionally" (Koller and Biary 1989; Lang 1991) and feels relief after its execution, whereas alien hand occurs unintentionally and without the patient's sensing any compulsion or relief.

Self-mutilation and other stereotypies that may occur in autism, Lesch-Nyhan disease, and frontotemporal dementia (Mendez et al 1997) are distinguished from alien hand in that they include whole-body activities rather than one limb and, thus, they do not involve a depersonalized regard for the limb. However, potentially self-injurious behavior has been reported in alien hand, such as choking and slapping (Goldstein 1908; Puccetti 1989).

Similar to frontal alien hand is “magnetic misreaching,” wherein the patient cannot touch an object in peripheral vision and instead deviates towards a centrally-fixated target, despite clearly understanding the task requirements (Carey et al 1997). This disorder is associated with bilateral parietal disease. It differs from frontal alien hand in that no compulsive reaching is seen.

A kind of "anti-alien hand" has been reported and termed “avoidant reaction” (Denny-Brown et al 1952; Denny-Brown 1958; Lechevalier et al 1977; Nagumo et al 1993; Hoogenraad et al 1994). In avoidant reaction, the patient's fingers extend and the arm rises on the approach of the examiner, rather than grasping at the examiner. This disturbance follows parietal lobe injury and was suggested to occur from a loss of inhibition from frontal and temporal regions that effect withdrawal from environmental stimuli (Denny-Brown 1956).

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## Diagnostic workup

The diagnosis of alien hand may facilitate determining the site of injury and its etiology. When the patient complains of involuntary limb activity, the behavior should be accurately described or demonstrated by the patient or viewed by the examiner. Limb movements that appear to be dissociated from the patient's plan, or that are inappropriate for the circumstances, should be examined more carefully. Goal-directed or seemingly purposeful activity that the patient denies causing suggests alien hand. Detailed neurologic examination can indicate the subtype of alien hand. Reflexive grasping or absence of spontaneous speech suggests the frontal variant following medial frontal injury. Tactile anomia and ideomotor apraxia of the nondominant hand suggests a callosal lesion. Hemianesthesia suggests that the sensory alien hand variant may be involved, following posterior cerebral hemispheric injury.

Following a thorough neurologic examination, cerebral neuroimaging should be performed to localize the injury and identify its pathology and etiology. In spontaneous alien hand, cerebral infarction is commonly responsible. The frontal variant is often due to rupture of an anterior communicating artery aneurysm and, therefore, angiography should be considered when neuroimaging fails to indicate the site or source of injury. The callosal variant may follow spontaneous infarction but is also frequently seen after surgical corpus callosotomy to treat refractory epilepsy. In recent years, corpus callosotomy has been limited to a portion of the callosum to minimize the occurrence of alien hand and other disconnection impairments. Alien hand associated with ipsilateral somatosensory dysfunction should prompt evaluation of the contralateral posterior cerebral hemisphere for infarction or other lesion. Interestingly, alien hand has not been observed in developmental callosal disorders such as callosal agenesis (Della Sala et al 1994); this suggests that adult-onset disorders are required for its production.

Dementing, degenerative cerebral disease may also be associated with alien hand, including cortical-basal ganglionic degeneration (Gibb et al 1990; Riley et al 1990), Alzheimer disease (Ball et al 1993; Green et al 1995), sudanophilic leukodystrophy (Kaufer et al 1996), Creutzfeldt-Jakob disease (MacGowan et al 1997; Inzelberg et al 2000; Colomer Rubio et al 2001), and Marchiafava-Bignami disease (Rosa et al 1991; Caparros-Lefebvre et al 1995). Brain neuroimaging is again indicated. Depending on the clinical presentation, diagnosis may be made through assessing the history, neuroimaging findings, and possibly brain biopsy.

Alien hand may occur as a couple of restricted episodes rather than recur frequently. Mechanisms proposed to account for such phenomena have been epileptic seizures (Leiguarda et al 1993) and transient ischemic attack (Andre and Domingues 1996), because the phenomena were accompanied by other features suggesting these disorders. In such cases, a workup is indicated for assessing epilepsy and cerebrovascular ischemia (electroencephalography, carotid duplex scanning, etc.).

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## Prognosis and complications

When alien hand originates from focal injury of acute onset, recovery generally occurs within a year (Goldberg and Bloom 1990; Papagno and Marsile 1995; Chan and Ross 1997). However, exceptions exist. One case of alien hand that occurred following cerebral gunshot wound to the callosum persisted for 12 years, until the patient died of nonneurologic disease (Banks et al 1989). Other reports have described intermanual conflict for as long as 3 to 4 years after cerebral injury (Ferguson et al 1985; Cantagallo and Boldrini 1997).

In contrast to acute focal injury, alien hand associated with progressive degenerative cerebral disorder may persist until the patient dies or until the cerebral degeneration is so advanced that it interferes with limb mobilization (Doody and Jankovic 1992).

Alien hand generally does not pose risks. Potentially self-injurious behaviors by the hand have been reported, such as self-slapping and self-choking (Goldstein 1908; Puccetti 1989; MacGowan et al 1997; Pack et al 2002), but these phenomena have not been noted to cause serious injury. Unwanted violent actions directed toward the examiner were reported in one case of frontal alien hand (River et al 1995). The alien hand's grasping a hot utensil (Goldberg and Bloom 1990; Gottlieb et al 1992) or a sharp or self-powered tool, particularly an automobile steering wheel (Gottlieb et al 1992; Leiguarda et al 1993), obviously risks great injury to the patient and must be avoided. Compulsive grasping has also been associated with self-directed skin abrasion (Goldberg and Bloom 1990).

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## Management

Rehabilitation for the alien hand syndrome has not been developed (Gottlieb et al 1992). One patient's alien hand interfered so much with daily activities "that his left hand had to be secured to the bed" (Starkstein et al 1990). In a case of the frontal alien hand variant, an oven mitt applied to the errant left hand completely abolished compulsive grasping (Nicholas et al 1998; Ortega-Albas et al 2003). Other instances of frontal alien hand responded well to constant visual or tactile contact, including warm water application (Goldberg and Bloom 1990) or pocketing (Kikkert et al 2006). Perhaps the frontal variant is generally inhibited by constant visual or tactile feedback. This hypothesis is supported by the observation that voluntary rhythmic limb movement can inhibit the frontal alien hand variant (Brainin 2005). Modifications of the patient's environment to reduce fatigue and near by distractors potentially could help to control the behavior (Giovannetti et al 2005).

These approaches cannot be considered therapeutic but may be necessary to prevent injury. One study has found that an annoying alarm activated by EMG biofeedback may reduce the time the frontal alien hand spends holding an object (Wu et al 1999), but it is unclear that the procedure actually reduces disinhibited grasping itself.

Because a patient with the frontal alien hand variant showed improved control when concentrating on the limb, one study viewed the disorder as possibly secondary to an attentional disturbance and, therefore, attempted to treat the disorder with methylphenidate up to 30 mg per day in a double-blind, placebo-controlled fashion (Mark et al 1991). However, the patient did not benefit. Amantadine 200 mg per day has been reported to benefit utilization behavior in a single case (Suzuki et al 1992) and, therefore, might improve the frontal alien hand variant. Levodopa was used in an attempt to treat alien limb in a case of cortical-basal ganglionic degeneration, but the patient did not benefit (Kompoliti et al 1998).

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## Associated disorders

Marchiafava-Bignami disease
Sudanophilic leukodystrophy
Cortical-basal ganglionic degeneration
Creutzfeldt-Jakob disease
Cerebral infarction

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## Related summaries

Alzheimer disease
Anterior cerebral artery stroke syndromes
Creutzfeldt-Jakob disease
Neglect
Rostral brainstem and thalamic infarctions

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## Differential diagnosis

focal cerebral injury
degenerative dementing cerebral disorders
dystonia
hemiballism
unilateral intention tremor
parkinsonism
chorea
cortical-basal ganglionic degeneration
progressive supranuclear palsy
seizures
cortical reflex myoclonus
action tremor
psychogenic dystonia
synkinesis
mirror writing
Klippel-Feil syndrome
Kallmann syndrome
dissociative personality disorder
delusional disturbances
attentional disturbances
somatoparaphrenia
asomatognosia
facilitory paratonia
unilateral ideomotor apraxia
graphic disconnection syndrome
autism
obsessive-compulsive disorder
Lesch-Nyhan disease
multiple personality disorder
paroxysmal dyskinesia
partial complex seizure disorder
REM sleep behavior disorder
sleep-related eating disorder
sleepwalking
Tourette syndrome

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## Demographics

For more specific demographic information, see the Epidemiology, Etiology, and Pathogenesis and pathophysiology sections of this clinical summary.

### Age

19-44 years
45-64 years
65+ years

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