What do we know about delusional misidentification disorders? A focus on Capgras syndrome

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Practice points

- Capgras syndrome is a delusional misidentification, where an individual perceives that a spouse, relative, friend, pet, object or even oneself is replaced by an imposter.

- A disconnection between the inferior temporal cortex and the amygdala may result in this delusional misidentification.

- Misidentification syndromes can be associated with neurological disorders such as dementia, cerebral infarction, postictal delirium, traumatic brain injury and multiple sclerosis.

- Delusional misidentifications are reported in patients with drug toxicities, alcohol intoxication, metabolic conditions and nutritional deficiencies.

- Capgras syndrome is documented in mental illnesses such as schizophrenia, schizoaffective disorders and depression.

- A comprehensive evaluation for the underlying etiology is necessary for all persons experiencing delusional misidentifications.

- Treatment is directed towards the causative pathology. Antipsychotic medications may be beneficial as a primary or adjunctive therapy. Psychotherapy might also be helpful.

SUMMARY There are numerous conditions with delusional misidentifications, among them being Capgras syndrome. This presentation is characterized by a false belief that an imposter has replaced someone, usually a family member or other person close to that individual. Capgras syndrome can be caused by dysfunction between the temporal cortex and the amygdala and is often reported to be associated with neurologic, metabolic and/or psychiatric illnesses. It is also observed with medication, alcohol or other substance toxicities. Upon completing a diagnostic workup, treatment is directed towards the etiology and relief of psychotonic symptoms.
Capgras syndrome (CS) is a misidentification disorder in which people exhibit a delusion that a spouse, parent, friend, or other person has been replaced by an imposter [1]. This type of delusion is named after Jean Marie Joseph Capgras (1873–1950), a French psychiatrist, who first reported this condition in 1923 [2]. He described a woman who complained that a 'double' had replaced her husband; this presentation was called the illusion of doubles. Beyond cases described about people, Capgras has also been reported with pets being 'replaced' by another animal [3]. CS is documented in patients with delusional misidentification of inanimate objects, such as a pair of glasses or a road sign being replaced by a similar looking double [4,5].

Capgras delusions can present due to brain disorders, trauma, metabolic disturbances, toxicities, functional mental illnesses or it can occur without an identifiable cause [6]. Psychodynamic theories have been proposed to explain how people can manifest these false, psychotic beliefs, but considerable evidence favors an organic etiology [7].

Two individuals with CS are described in order to illustrate some of its various presentations, etiologies, pathophysiologies and treatments. Since this delusion can occur in persons with functional illnesses and in those with organic ailments, it is important to always determine the cause of the abnormal thinking. The two cases depict some of this spectrum. With proper diagnosis and treatment, both patients recovered with no further misidentifications.

Clinical vignettes

Case 1
A 65-year-old female was hospitalized for mental status changes and refusal to eat. She had lost over 20 pounds and presented with anorexia and depression. She was sad, isolative, tearful and had lost her appetite. The history and physical examination were otherwise non-diagnostic. There was no past history of psychiatric illness or mental health problem. A medical assessment was negative for gastrointestinal pathology. Computerized tomography and MRI of the head were significant only for atrophy consistent with the patient’s age. An EEG revealed normal background rhythm without epileptic foci. In addition to anemia, laboratory studies were consistent with her decreased fluid and nutritional intake, including elevated blood urea nitrogen and urine specific gravity. There was no evidence of neurological pathology. Because of her depression, a psychiatric consultation was obtained.

Her husband of 40 years was at her bedside, but the patient refused to talk in his presence. Upon his departure, she explained that she did not recognize that man in her room; this presentation was called the illusion of doubles. Beyond cases described about people, Capgras has also been reported with pets being 'replaced' by another animal [3]. CS is documented in patients with delusional misidentification of inanimate objects, such as a pair of glasses or a road sign being replaced by a similar looking double [4,5].

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Case 2
A 34-year-old man with epilepsy, previously prescribed phenytoin and phenobarbital, discontinued his medications at the advice of a spiritual healer. Soon thereafter, he exhibited recurrent episodes of generalized seizures, each lasting for less than 5 min. His behavior and thinking were abnormal at the time of this presentation, exhibiting signs compatible with a delirium, as he was disoriented, muttering unintelligibly and grasping at things near him. He had no history of substance abuse or head injury. Primary psychotic conditions as well as mood disorders with psychotic features were considered as etiologies, but these were unlikely because he was newly confused and had never before experienced any mental health concerns. Neurological examination, blood tests, urinalysis and brain imaging were unremarkable. An EEG documented generalized ictal activity.

After anticonvulsant drugs were re-administered, he was transferred to inpatient psychiatry. On mental status examination, the patient was unkempt, uncooperative, disoriented and anxious. He continued the strange behaviors of the initial presentation. Furthermore, he thought...
that his wife and neighbors were imposters and he even refused food from his wife.

The patient was prescribed a daily regimen of valproic acid, risperidone and lorazepam. The next day he became cooperative but remained disoriented. The Capgras symptoms were unchanged. A second EEG evidenced no focal changes or epileptiform discharges. On the fifth hospital day, the patient became fully oriented and the delusions resolved. With this improvement, risperidone and lorazepam were discontinued. Valproic acid was maintained as the sole pharmacotherapy. His mental status remained normal, thus the diagnosis of postictal delirium secondary to epilepsy was retained.

Pathophysiology
The etiology of Capgras delusion is theorized to result from dysfunction of the inferior temporal cortex and amygdala [10]. The inferior temporal cortex is involved with facial recognition, and the amygdala is associated with the simultaneous emotional reaction to that observed person. These two structures can be damaged independently. If the ability to recognize faces remains intact, but the emotional reaction which makes them familiar is absent, the patient may conclude that the person in question is an imposter. Such phenomena might represent a form of prosopagnosia. In research subjects, a disconnection can occur between the temporal cortex and the limbic system [8,9]. Facial recognition impairment and emotional responses are areas of physiologic interest [10–15].

Psychodynamic theories have attempted to explain Capgras misidentification phenomena. Displacement issues can surface so that unpleasant feelings are displaced to an imposter [16]. A splitting mechanism may present as a defense against a loss or distress in a relationship [16].

Neurological etiologies

Dementia
Neurodegenerative dementias account for 81% of the patients with Capgras [17]. People with Alzheimer's disease sometimes have such misidentifications [18]. Inanimate object misrecognitions are also reported in dementia cases [19]. This type of object confusion may be referred to as a reduplicative paramnesia. Coexistence of dementia and Capgras symptoms worsens health concerns, hastens early nursing home placements and is upsetting to families [17]. CS is also observed in demented persons with Parkinson's disease. Treatment with l-DOPA may diminish these misperceptions in these individuals [20]. In addition, CS is documented in patients with Lewy body dementia [21].

CS is also a complication of hypertension-induced vascular dementias [22]. Delusions, especially in the initial stages of the disease, are distressing for patients and their relatives [23]. This condition in a demented individual mandates prompt recognition with a thorough evaluation to detect the primary pathology. The underlying cause of the dementia must be treated and the delusional features may respond to antipsychotic drugs.

Cerebral infarction
CS has been reported in a patient with watershed cerebral infarct ischemia [24]. These cases are uncommon, but can be identified by brain imaging. Visual misidentifications are also associated with posterior watershed infarctions of the right posterior cerebral region [25].

Postictal delirium
Up to 10% of people in a postictal state may exhibit a psychosis [26], but only a fraction of them experience delusional misidentifications [27]. Yet, CS is reported during the postictal period of generalized, tonic-clonic or complex partial seizures [7]. It has been attributed to disinhibition or chemical changes in the dominant cerebral hemisphere responsible for image recognition, or an imbalance of nondominant hemisphere image perception [28–30]. It is occasionally documented in patients following an ictus induced by electroconvulsive therapy [31]. Treatment of postictal Capgras is directed towards the pathology causing the convulsion and at establishing seizure control [1]. With ictal control through the use of anticonvulsant drugs, these misrecognitions usually resolve.

Trauma
Brain injury [32,33] and subarachnoid hemorrhage [34] are documented with Capgras. Such misidentification syndromes tend to appear due to perceptual deficits and impaired consciousness following head trauma. Memory deficits and hallucinations are often more persistent.

Multiple sclerosis
There has been one reported case of Capgras delusions in a person with multiple sclerosis [35]. A patient with bipolar disorder and multiple...
sclerosis presented with misrecognition delusions during an acute relapse of neurological dysfunction. She responded to treatment with antipsychotic medication.

- **Fahr’s disease**
  In Fahr’s disease, idiopathic, bilateral basal ganglia calcifications result in brain circuit pathology [36]. This cerebral disorder manifests in a psychosis with auditory or visual hallucinations and delusions with dysfunction in facial recognition.

- **Toxicities**
  - **Drugs**
    Several medications may cause a transient CS, including diazepam [37], lithium [38] and morphine [39]. Such symptomatology was reported in a woman after being administered ketamine, an antagonist of N-methyl-D-aspartate receptors [40]. Reportedly, ketamine exposure has induced other misidentification presentations that result in right frontal cortex dysfunction and similar delusional thinking [41].

  - **Alcohol**
    While not a direct cause of CS, alcohol intoxication in mentally ill people occasionally precipitates violence towards family members who become the subject of delusional misidentifications [42]. There are several reports of such dangerousness [43,44].

- **Metabolism**
  In diabetic patients, symptoms of CS are documented during periods of hyperglycemia [45]. Functional cerebral reserve is compromised by an elevated blood glucose, and affected individuals may experience intermittent, fluctuating episodes of such delusions during hyperglycemic episodes. Pseudohypoparathyroidism [46] and myxedema [47] can occasionally create clinical misidentifications. The same might apply to nutritional deficiencies, such as folate insufficiency [48,49].

- **Psychiatric illness**
  Though unusual itself, most cases of CS are commonly associated with psychotic diagnoses, such as schizophrenia and schizoaffective disorder [50]. Mentally ill persons can exhibit delusional misidentifications that are a sign of psychotic thinking and are noted in a variety of psychotic diagnoses, including mood disorders. Patients suffering from CS secondary to a psychosis tend to misidentify people who are emotionally close to them [51]. CS is also reported in cases of misidentification by patients to themselves [52]. Antipsychotic medicines are frequently employed in their treatment. While Capgras does occur in these functional conditions, neurological etiologies should always be ruled out by completing a thorough diagnostic evaluation.

  A Fregoli delusion is a related misidentification syndrome that has been reported to occur in a patient with CS [50,51]. It is observed in patients with misrecognition of strangers, believing them to be a familiar person [54]. There are two other related and similar misidentification conditions: intermetamorphosis and the delusion of subjective doubles. Intermetamorphosis is a presentation wherein patients believe that they can see others changing into someone else by altering their appearance and personality [55]. A delusion of subjective doubles is a misidentification in people who feel that they have a double who looks the same as they do, but has a different personality and lifestyle [56].

### Evaluation & treatment

Patients with CS must receive a complete assessment [1]. Evaluation focuses on neurological, metabolic, drug or other substance usage, and psychiatric pathologies. Brain imaging, electroencephalography or other studies are often indicated in an individualized clinical appraisal. The primary treatment is directed at the causative pathology [7]. Antipsychotic pharmaceuticals are often symptomatically applied.

There is a reported case of CS successfully treated with pimozide pharmacotherapy [57]. This patient’s symptoms resolved while taking pimozide after failing to improve following the use of other antipsychotic drugs prescribed for a month. Another clinical vignette noted a successful intervention with mirtazapine [58]. A Parkinson’s disease patient with Capgras was documented to have benefited following electroconvulsive therapy together with antipsychotic drugs [59].

Psychotherapy can help patients and their families cope with the stress of misidentification [51]. Since CS usually presents comorbid with other conditions, its treatment is frequently multidisciplinary and mandates open physician intercommunication.
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- of interest
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