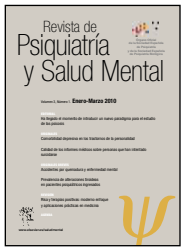
Rev Psiquiatr Salud Ment (Barc.) 2011;**4(2)**:96–100

Revista de Psiquiatría y Salud Mental

www.elsevier.es/saludmental



BRIEF ORIGINAL

Capgras Syndrome associated with the use of psychoactive substances

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Received September 24, 2010; accepted February 14, 2011

KEYWORDS
Capgras syndrome;
Facial processing;
Prosopagnosia;
Frontotemporal cortex;
Substance abuse

Abstract
Introduction: Capgras syndrome has originally been described as psychiatric syndrome. However, in the last few years reports of patients with this syndrome has significantly increased in patients with neurological, metabolic, and infectious diseases and those who consume alcohol. Different hypotheses have been proposed to explain the neurobiology of this very unusual symptom, such as changes in the dopamine circuit and specific dysfunctions in facial processing.
Case: In this work we present a new case of Capgras syndrome, associated with an acute cocaine overdose, which was transient and reversible.
Discussion: The neurobiological bases of this syndrome are analysed, along with their relationship with the changes induced by cocaine use. Thus, Capgras syndrome could be the expression of functional changes at frontal-temporal level, and the paralimbic region secondary to the consumption of psychoactive substances such as cocaine.

PALABRAS CLAVE
Síndrome de Capgras;
Procesamiento de rostros;
Prosopagnosia;
Corteza frontotemporal;
Abuso de sustancias

Síndrome de Capgras asociado al consumo de sustancias psicoactivas

Resumen
Introducción: El síndrome de Capgras ha sido descrito originariamente como un síntoma psiquiátrico, sin embargo en los últimos años se han incrementado notablemente los reportes de pacientes con este síndrome entre pacientes con enfermedades neurológicas, metabólicas, infecciosas y consumo de alcohol. Se han propuesto diferentes hipótesis para explicar la neurobiología de este síntoma tan particular, alteraciones en el circuito de la dopamina y disfunciones específicas en el procesamiento de los rostros.
Caso: En este trabajo se presenta un caso nuevo de síndrome de Capgras asociado a la intoxicación aguda por cocaína, de tipo transitorio y reversible.
Discusión: Se analizan las bases neurobiológicas de dicho síndrome y su correlación con las alteraciones secundarias al consumo de cocaína. Así, el síndrome de Capgras podría ser la expresión de alteraciones funcionales a nivel frontotemporal y la región paralímbica secundarias al consumo de sustancias psicoactivas como la cocaína.

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1888-9891/$ - see front matter

Introduction

The *delirio de Sosias* [literally, Sosias delusion], or Capgras syndrome (CS) in English, owes its name to one of the characters in the mythological comedy *Amphitryon* by Plautus.[a] The Spanish term *sosias*, based on this play, is used to describe "a person who resembles someone else to the point that he could be confused with that person."[b] The term has its analogue in the French word *sosie*, as well. In 1923, J. Capgras and J. Reboul-Lachaux reported the case of a patient, Mme. M., who presented with symptoms of chronic delusional psychosis with ideas of persecution and grandeur that included relatives who owned mines in Buenos Aires, claiming that some of her relatives had been replaced.[1] Prior to these reports, authors such as Kahlbaum (1866), Magnan (1893), and Janet (1903) had described similar symptoms.

The clinical picture is characterised by the recurrent delusional belief that someone, usually from the patient's immediate environment, has been replaced by an impostor. In general, patients describe imperceptible differences between the original person and the impostor. In other words, the impostor is physically identical to the family member who has been replaced but is not that person.

The question is raised as to whether this clinical picture should be considered an isolated syndrome or a symptom that may be part of other pathologies. Generally speaking, case reports support the idea that it would be a symptom that may be present in various psychiatric and neurological disorders or even in the context of metabolic diseases.

Variations of CS have been described, such as *Fregoli syndrome*, where delusional patients identify a relative in some other person. In this case, the relative's "personality" has invaded the stranger while the stranger has retained his own physiognomy. Here, the physiognomy is different from that of the relative—and clearly recognised by the patient—but the delusional belief is that the relative's "personality" has taken over the stranger's body.[2] The *syndrome of intermetamorphosis* has also been described, where the patient has the delusional conviction that people around him are changing their appearance so that they look like other people,[3] as well as the *syndrome of subjective doubles*, where the patient himself psychically transforms a stranger, adopting his identity and physiognomy.[4]

Even though, historically, CS had been associated only with psychiatric pathologies, such as paranoid schizophrenia,[5-7] schizoaffective disorder[8] or mood disorders,[9] and as an extremely rare clinical manifestation, in recent years, cases of this syndrome have been reported in multiple and different pathologies,[9] such as epilepsy,[10] cerebrovascular accident,[11-13] head injury, brain tumours, degenerative diseases such as Alzheimer's disease[14-16] or Lewy body dementia,[16,17] multiple sclerosis,[18] Parkinson's disease,[19] metabolic diseases,[13] infectious diseases,[20] and intoxication with abused substances,[16] among others.

It is estimated that CS occurs in approximately 4% of psychotic patients, the majority of whom have paranoid schizophrenia, and in 20%-30% of patients with Alzheimer's disease.

The objective of this article is to analyse the various neurobiological hypotheses that have been proposed and relate them to a case reported where CS occurred in the context of acute cocaine intoxication, being a self-limited and reversible symptom. Although cases related to alcohol consumption have been reported,[21,22] as far as we know, this is the first case of CS associated with cocaine use.

Proposed neurobiological hypotheses for Capgras Syndrome

Multiple and quite varied hypotheses have been tested to explain how and why the double or *sosia* phenomenon occurs—from psychodynamic-psychoanalytical theories[23-25] to neurobiological and cognitive theories. The first hypotheses with a psychoanalytical slant evolved from the fact that the first reported cases of CS were in patients with psychiatric disorders. However, as this clinical picture was being reported in other diseases, such as Alzheimer's disease, multiple sclerosis, and head injury, new pathophysiological hypotheses have been proposed.

From a neurochemistry standpoint, it has been proposed that there is an underlying functional impairment in CS related to increased activity in the dopamine circuit.[19,26]

From the neuroanatomy point of view, CS has been associated with lesions of the right hemisphere; however, most studies have found bilateral impairment in the majority of patients.[27,28] The regions that have been associated with this syndrome are the frontal, temporal, and parietal lobes. Atrophy of the frontotemporal cortex was found in patients diagnosed with both schizophrenia and Alzheimer's-type dementia who presented with CS.[29] Functional neuroimaging studies (PET) found an impairment in glucose metabolism in the paralimbic region and the temporal lobe in patients with Alzheimer's-type dementia and CS.[30] Neuropsychological findings support a frontal dysfunction, since many patients with CS have test results inferior to those expected on frontal lobe assessment.[31] These findings should be interpreted with caution, however, because CS may be the clinical manifestation of another syndrome such as, for example, a paranoid schizophrenia disorder, Alzheimer's disease, or a temporal lobe epilepsy—syndromes that involve neuropsychological impairment *per se*, with or without CS. In other words, ancillary test results are useful for orientation, but it is impossible to conclude

[a] In this work, which dates from approximately 188 BC, the Roman author describes how Jupiter, who is in love with Alcmene, the wife of Amphitryon, takes on this man's figure in order to spend a night with her while Amphitryon was in the middle of a campaign against the Teleboans. In turn, Jupiter's son, Mercury, takes the form of Amphitryon's slave, Sosia, whom he replaces so he can guard the door of Alcmene's house and prevent anyone from entering the mansion while Jupiter, transformed into Amphitryon, is with Alcmene. The real Sosia returns, and Mercury keeps him from entering the house, so Sosia goes back to the harbour to tell his master, Amphitryon, what has happened. Amphitryon does not believe Sosia and treats him as if he were crazy.

[b] [direct quote from Spanish dictionary] Sosias (De Sosias, personaje de la comedia Anfitrión, de Plauto). 1. m. Persona que tiene parecido con otra hasta el punto de poder ser confundida con ella. [From] Diccionario de la *Real Academia Española* [Dictionary of the Spanish Royal Academy], twenty-second edition, on-line, available at www.rae.es

that they are pathognomonic for CS because CS does not occur in isolation but rather as part of another clinical picture.

Along this line, it has been proposed that this syndrome occurs due to a problem with correctly processing known faces. Some indicate that it would be an impairment in the integration of information between the right and left hemispheres.[32,33] Vigheto postulates that an injured right hemisphere would deprive the left hemisphere of proper information, rendering it unrestrained and resulting in the patient's delusional verbalisations.[34]

CS has been differentiated from another neurological syndrome known as prosopagnosia, in which the patient is unable to recognize familiar faces. In this syndrome, patients are able to recognize their relatives by voice, by the way they walk or the way they dress, and by their glasses or beard. Here, the lesion would be found in the right ventromedial occipito-temporal area. According to the face recognition model proposed by Bruce and Young, the impairment in prosopagnosia would be found at the level of *face recognition units*, while in CS, the impairment would be found in the *person identity nodes*—it would be an agnosia for identification with face recognition preserved.[35,36]

Ellis and Young proposed that, when looking at faces they recognize, CS patients do not feel the emotional content associated with those familiar faces. This would involve not a failure to recognize familiar faces but rather a failure of those faces to arouse personal meaning. So, there would be damage to the neural circuit responsible for linking a familiar visual stimulus and generating the emotional response to that stimulus. These authors point out that it would be a mirror phenomenon to prosopagnosia. Consequently, the patient with CS loses the sense of familiarity that known faces arouse in him because, in this phenomenon, the emotional connotations are not transmitted. This is why the patient reacts indifferently to his relatives, experiencing no emotion in their presence, and where the patient's explanation that they have been robbed of their identity originates.[24]

Hirstein and Ramachandran propose that, in CS, there would be a disconnect between the limbic system—the amygdala, specifically—and the inferior temporal cortex,[25,37] which is why patients would be unable to access the emotional memory associated with that relative. So, the delusion would arise as a response to the pathological situation of not experiencing a feeling of familiarity in the presence of a known face; thus, this is a family recognition agnosia with secondary delusional reduplication.[38]

Along this line, Ellis et al showed that, while patients with CS had an autonomic response that did not distinguish between familiar faces and unfamiliar faces, their response to familiar auditory stimuli was appropriate; in other words, patients were able to recognize their relatives when they were talking by phone.[39] This is somewhat different from what Damasio and Tranel reported for patients with prosopagnosia: that these patients had an autonomic response—dermal conductance—to the faces of people they knew but were unable to name. This dermal conductance response did not occur with unknown faces. So the authors propose that the patients with prosopagnosia knew those faces but were not aware of that, despite the fact that they were able to evidence an autonomic response.[40]

Bauer has proposed a double pathway for the processing of faces in the right hemisphere: a ventral pathway connecting the visual cortex (inferotemporal) to the hippocampus, the amygdala, and the fronto-orbital cortex, and another dorsal pathway connecting the visual cortex to the inferior parietal cortex, the cingulate gyrus, and the dorsolateral frontal cortex.[41] The first would be responsible for conscious processing, impairment of which would be associated with prosopagnosia; the second, the dorsal circuit, would be associated with CS and would be responsible for transmitting the emotional reaction to the face. Other authors have suggested a different neural circuit,[37,40] however, indicating an important role for the retrospinal cortex, as well, the fusiform gyrus.[42,43] Moreover, functional neuroimaging studies with PET in patients with Alzheimer's disease showed a dysfunction in the connection between the frontal and temporal lobes and the paralimbic region.[30,44] Along this line, a neuropathology study found limbic, paralimbic, and frontal dysfunctions in patients with Lewy body dementia associated with delusional identification;[45] a case of CS secondary to epilepsy surgery (temporal lobectomy) has also been reported.[46]

Presentation of the case

Patient was a 31-year-old male with an unremarkable medical history except for polyconsumption of psychoactive substances (marijuana, cocaine, alcohol, psycho-active drugs) since he was 20 years old. There was no known psychiatric history. The patient was taken to an Urgent Care service for symptoms of psychomotor agitation secondary to cocaine use. His wife reported that, after using cocaine, the patient assaulted her verbally, stating that she (his wife) was not his wife, that she was an impostor who had replaced his real wife. This situation was of a transitory nature and occurred only after his use of cocaine. Upon examination and after the treatment instituted, the patient's higher mental functions and the neurological examination were within normal limits.

Discussion

CS has been associated only with psychiatric pathology, such as paranoid schizophrenia, schizoaffective disorder, and mood disorders. In recent years, however, cases of this syndrome have been reported in connection with multiple and different pathologies: epilepsy, cerebrovascular accident, head injury, brain tumours, degenerative diseases such as Alzheimer's disease or Lewy body dementia,[17] multiple sclerosis,[18] metabolic diseases,[13] infectious diseases,[20] and intoxication with abused substances.[16] Although there has been indication of it being associated with the use of psychoactive substances, specific cases involving this association have not been reported. In this regard, in the case presented, the presence of neurological and chronic psychiatric pathology was ruled out, the CS

presenting as the result of an acute cocaine intoxication that was transitory and reversible in nature. Thus, CS secondary to acute cocaine intoxication may be explained in neurobiological terms, since cocaine users have been shown to have prefrontal cortex, temporal—the amygdala—parietal, and insular impairments.[47] From a neurochemistry standpoint, it has been proposed that hyperactivation of the dopaminergic circuit would be associated with CS. Therefore, it is neurobiology that, in the absence of neurological and psychiatric pathology, would explain a case of transitory and reversible CS secondary to acute cocaine intoxication.

Conflict of interest

The author declares that he has no conflict of interest.

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