Cotard’s Syndrome

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ABSTRACT

Cotard’s syndrome is characterized by nihilistic delusions focused on the individual’s body including loss of body parts, being dead, or not existing at all. The syndrome as such is neither mentioned in DSM-IV-TR nor in ICD-10. There is growing unanimity that Cotard’s syndrome with its typical nihilistic delusions externalizes an underlying disorder. Despite the fact that Cotard’s syndrome is not a diagnostic entity in our current classification systems, recognition of the syndrome and a specific approach toward the patient is mandatory.

This paper overviews the historical aspects, clinical characteristics, classification, epidemiology, and etiological issues and includes recent views on pathogenesis and neuroimaging. A short overview of treatment options will be discussed.

Keywords: Cotard’s syndrome, nihilistic delusion, misidentification syndrome, review

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INTRODUCTION: HISTORICAL ASPECTS AND CLASSIFICATION

Cotard’s syndrome is named after Jules Cotard (1840–1889), a French neurologist who described this condition for the first time in 1880, in a case report of a 43-year-old woman. Mss X, affirms she has no brain, no nerves, no chest, no stomach, no intestines; there’s only skin and bones of a decomposing body. . . . She has no soul, God does not exist, neither the devil. She’s nothing more than a decomposing body, and has no need to eat for living, she cannot die a natural death, she exists eternally if she’s not burned, the fire will be the only solution for her. (Translation from Cotard 1880)1

Cotard formulated a new type of depression, characterized by anxious melancholia, ideas of damnation or rejection, insensitivity to pain, delusions of nonexistence concerning one’s own body, and delusions of immortality. He categorized this under lypomanie, a kind of psychotic depression, based on the analogy with five cases described in 1838 by Esquirol.2 Later, Cotard introduced délire des negations as new terminology for the syndrome.3 The eponym Cotard’s syndrome was introduced in 1887 by Séglas.4 A few years later, Régis stated that the syndrome (he named it délire de Cotard) was not only associated with depression, but might be linked to other psychiatric disorders as well.4

Two components of the syndrome were defined by Tissot: an affective component associated with anxiety and a cognitive component associated with the presence of delusion.5 Loudet and Martinez6 made a first attempt to classify different types of the syndrome. They described a nongeneralized délire des negations, associated with paralysis, alcoholic psychosis, dementia, and the “real” Cotard’s syndrome, only found in anxious melancholia and chronic hypochondria.6 Later, in 1968, Saavedra proposed a classification into three types: depressive, mixed, and schizophrenic. He drew a distinction between a “genuine” Cotard’s syndrome occurring during depressive states and what he described as a pseudonihilistic or pseudo-Cotard syndrome classified as “co-anaesthetic schizophrenic.”7

In 1995, for the first time, a classification was made on evidence basis. In a retrospective factor analysis of 100 cases in literature, Berrios and Luque subdivided Cotard’s syndrome into three types. A first type included a form of psychotic depression, characterized by anxiety, melancholic delusions of guilt, and auditory hallucinations. A second type, described as Cotard’s syndrome type I, was associated with hypochondriac and nihilistic delusions and absence of depressive episodes. The third group was the Cotard’s syndrome type II, with anxiety, depression, auditory hallucinations, delusions of immortality, nihilistic delusions, and suicidal behavior as characteristic features.8

Cotard’s syndrome is currently not classified as a separate disorder in DSM-IV-TR and ICD-10. In DSM-IV-TR, nihilistic delusions are categorized as mood congruent delusions within a depressive episode with psychotic features.9 Classifying Cotard’s syndrome as a separate entity is an extremely difficult exercise in our current diagnostic classification system.

METHODS

For this article, we started from the search results for “Cotard syndrome,” “Cotard’s syndrome,” and “nihilistic
delusion(s)\(^1\) using PubMed and Web of Science. Relevant articles in English, French, Dutch, and German were gathered. Since data on this topic is scarce, we looked at every article for relevant cross references. A general Internet search on Google was also used. From this last result, we only included articles written in peer-reviewed journals. Using this method, we tried to obtain all available peer-reviewed data on this topic. This was necessary because there are no controlled studies available. All literature is dominated by case studies and some case series.

PRESENTATION AND COURSE

As described earlier, nihilistic delusions concerning the individual’s body are the central features of Cotard’s syndrome. In an analysis of 100 cases, the most prominent symptoms in Cotard’s syndrome are: depressive mood (89%), nihilistic delusions concerning one’s own existence (69%), anxiety (65%), delusions of guilt (64%), delusions of immortality (55%), and hypochondriac delusions (58%).\(^8\)

Some case reports concerning delusional denial of pregnancy despite clear morphologic signs\(^10\) and delusional paralysis in a patient with psychomotor agitation\(^11\) are reported as a special form of Cotard’s syndrome. However, the classification of these delusions as nihilistic delusions concerning one’s body can be debated.

A classical description of the course of Cotard’s syndrome is given by Enoch and Trethowan. In its early stages, Cotard’s syndrome is characterized by a vague feeling of anxiety, with a varying time span from weeks to years. This anxious state gradually augments and can result in nihilistic delusions where denial of life or denial of body parts are the prominent features. The patient looses sense of reality.\(^12\) Despite the delusion of being dead, these patients show an increased tendency to automutilation or suicidal behavior. Additional symptoms may include analgesia and mutism. The core symptoms always reflect a preoccupation with guilt, despair, and death.\(^12\) Delusions can be accompanied by a délit d’énormité, a delusion of massive increase of body measures. This has been described as the manic Cotard’s syndrome.\(^12\) As the syndrome often occurs in association with other psychotic states, symptoms of these specific disorders are likely to be present. As an example, nihilistic delusions grafted on a depressive illness are often associated by other characteristics of a depressive episode such as weight loss and sleeping difficulties and the syndrome associated with organic disease is often associated with other symptoms such as disorientation or neurological signs.\(^12\) The duration of the syndrome can vary from weeks to years depending on the underlying disorder.\(^13\)

In 1999, Yamada et al\(^14\) made a proposal for staging Cotard’s syndrome. Based on a case report, he defined three stages: germination stage, blooming stage, and chronic stage. The germination stage is characterized by important hypochondria, cenesthopathy, and depressive mood. A diagnosis of Cotard’s syndrome cannot be made in this stage yet. In the blooming stage, the characteristic features of Cotard’s syndrome (nihilistic delusions, delusions of immortality together with anxiety and negativism) are seen. The last stage, the chronic stage is differentiated in two forms: one with persistent emotional disturbances (depressive type) and a second where depressive symptoms are less prominent (paranoid type).\(^15\) This hypothesis was supported in a second case report.\(^15\)

EPIDEMIOLOGY

The prevalence and incidence of this rare syndrome is not known. Only one study reported on prevalence in a selected psychogeriatric population in Hong Kong. In 2 out of 349 patients, Cotard’s syndrome was diagnosed suggesting a prevalence of .57% in this population. A prevalence of 3.2% was reached when severely depressed elderly were included.\(^16\) A recent study found .62% (n = 3) of patients in a Mexican sample (screened over a 2-year period) of primary psychiatric patients having Cotard’s syndrome.\(^17\) Using the same methodology they found also .11% (n = 1) having Cotard’s syndrome in a sample of neurological patients with mental disturbances.\(^17\) The likelihood of developing Cotard’s delusional syndrome appears to increase with age.\(^18\) Berrios and Luque\(^8\) found a mean age of 56 years in their analysis of 100 cases. A more recent study of 138 cases reported a mean age of 47.7 years.\(^19\) Women appear to be more vulnerable.\(^12\) The syndrome is found in different ethnic groups.\(^18\) Cotard’s syndrome is also occasionally described in children and adolescents.\(^19\) Diagnosis of Cotard’s syndrome in people under 25 years old was described to be associated with bipolar disorder.\(^19\)

Since Cotard’s syndrome is conceptualized as part of an underlying disorder, several psychiatric and somatic diseases have been associated with the syndrome. Unipolar\(^20,22,24,31-44\) or bipolar\(^12,14,15,19,25,29,45-49\) depression are the most common associated psychiatric disorders but also comorbid psychotic disorders\(^12,13,15,27,45-49\) has been reported. Some studies reported on the occurrence of Cotard’s syndrome with more uncommon psychiatric syndromes (hydrophobia,\(^41\) lycanthropy,\(^48\) folie a deux,\(^54\) Capgras delusion,\(^12,21,51-54,55-56\) Capgras and Fregoli delusion,\(^39\) depersonalization disorder\(^77\)). Also Parkinsonian symptoms, disappearing with successful treatment, are described.\(^77\) Several organic conditions were also associated: dementia,\(^13,57\) major depressive episode in mild cognitive impairment,\(^46\) depression in frontotemporal atrophy,\(^28\) severe mental retardation,\(^59\) typhoid fever,\(^56\) cerebral infarction,\(^64\) superior sagittal sinus thrombosis,\(^62\) brain tumors,\(^63\) temporal lobe epilepsy,\(^60,64\) limbic epileptic insults,\(^64\) postictal depression,\(^28\) cerebral arteriovenous malformation,\(^65\) cerebral arteriovenous malformation and epilepsy,\(^61\) migraine,\(^66\) Laurence-Moon-Bardet-Biedl syndrome,\(^57\) multiple sclerosis,\(^65\) Parkinson’s disease,\(^68,69\) brain injury,\(^70-72\) a noninfectious complication of heart transplantation\(^73\) as a consequence of an adverse drug reaction to aciclovir and its prodrug valaciclovir\(^24\) and in herpetic\(^77\) and nonherpetic\(^57\) encephalitis.
ETIOLOGY AND PATHOGENESIS

Neuroimaging

The first structural imaging study was performed in 1986, using Computed Tomography (CT). An association of Cotard’s syndrome with multifocal brain atrophy and inter-hemispheric enlargement was suggested.\textsuperscript{75} Others have described an enlargement of the third and lateral ventricle,\textsuperscript{50} a specific lesion to the temporoparietal areas,\textsuperscript{65} and changes in the nondominant temporoparietal areas, sometimes together with frontal damage.\textsuperscript{72} In general, these studies point to an important role for the fronto–temporo–parietal circuitry in the pathophysiology of the syndrome. However, in most cases, gross structural changes on structural brain imaging were absent.\textsuperscript{70}

Several functional imaging studies in Cotard’s syndrome patients were published. A dopamine D2 receptor SPECT study with $^{123}$I-iodobenzamide (IBZM), performed in one patient, showed an asymmetric striatal D$_2$ receptor binding in favor of the left hemisphere. These SPECT-findings persisted after remission. In this specific patient, no perfusion alterations were found with $^{99m}$Tc-hexamethylpropylenamide oxime (HMPAO) SPECT before treatment.\textsuperscript{33} Several, but not all, case studies reported decreased perfusion in several cortical areas measured with the same perfusion SPECT tracer. In one patient, a left-sided hypoperfusion in temporal, parietal, and frontal lobes was found with full recovery of the left inferior frontal hypoperfusion and minimal remaining hypoperfusion in the left temporal lobe after successful treatment using electroconvulsive therapy (ECT).\textsuperscript{59} A similar recovery of perfusion was found in another patient after ECT-treatment in the medial parietal cortex, medial and dorsolateral prefrontal cortex, the basal ganglia, and thalamus.\textsuperscript{42} Successful treatment with ECT in a patient with underlying major depressive disorder resulted in recovery of left and right temporal hypoperfusion\textsuperscript{46} and normalization of perfusion in the frontal cortex was reported after treatment with antidepressants.\textsuperscript{35} In one patient, severe right hemispheric dysfunction on neuropsychological tasks was not accompanied by perfusion abnormalities measured with $^{99m}$Tc Ethyl Cysteine Dimer (ECD) SPECT.\textsuperscript{45}

Psychological and Neuropsychological Factors

A depersonalization phenomenon was reported as an essential step in the development of Cotard’s syndrome by Séglas (1887).\textsuperscript{3} Alheid elaborated depersonalization in the Cotard’s syndrome context using the German terminology “Leib” (body for me) and “Körper” (body as such). Depersonalization may occur when “Körper” prevails over “Leib” and when the body is less associated with the self (Leib). However, in depersonalization the patient feels like being dead (indifference of affect), while in Cotard’s syndrome the patient is convinced to be dead (lack of feeling).\textsuperscript{7,12}

In the development of bizarre psychiatric syndromes related to parietal brain dysfunction, Critchley stated that the role of premorbid personality characteristics is essential.\textsuperscript{12} With regard to this premorbid personality characteristic, it is proposed that in Cotard’s syndrome, patients with a more internal attributional style (which is often co-occurring with depression) are more vulnerable to develop the syndrome. While patients with a more external attributional style (which is more co-occurring with paranoia) are more prone to develop Capgras’s syndrome (a delusion where familiar persons are replaced by identical impostors).\textsuperscript{78} This hypothesis that Cotard’s patients have a more internal attributional style was empirically tested in one case.\textsuperscript{77} A significant higher score on two attribution bias indices (internalizing bias index, internalizing bias for negative events) calculated on the IPSAQ (Internal, Personal, and Situational Attributes Questionnaire) was found in this patient with Cotard’s syndrome compared to control subjects.\textsuperscript{77} However, several authors reported the co-occurrence of both Cotard’s syndrome and Capgras’s syndromes.\textsuperscript{12,21,51,54,56} Vinkers suggested that a combination of attribution styles occur in these patients, in so far that these patients are both depressed and paranoid or that they suffer from delusions about self-identity and about identity of others.\textsuperscript{78} Unfortunately, evidence-based proof for this hypothesis is lacking.

The origin of both syndromes (and other delusional misidentification syndromes) is supposed to be related to a dysfunction of an information processing subsystem where face and body recognition is associated with recognition of familiarity. When a feeling of familiarity is absent, the patients may experience a feeling of derealization and depersonalization.\textsuperscript{79} This hypothesis is supported by several studies for a number of misidentification syndromes and especially for Capgras’s syndrome.\textsuperscript{80-82} Interestingly, in studies on face recognition tasks with skin conductance as outcome measure the differential autonomic response to familiar faces compared to unknown faces is absent in patients with Capgras’s syndrome.\textsuperscript{80,81} Another patient with atypical Capgras’s delusion showed impaired interpretation of facial expressions. This leads to mistake differences in expression for differences in identity.\textsuperscript{82} For Cotard’s syndrome, a lack of differential autonomic response to anything is suggested. This can lead to the delusion of being dead, where in Capgras’s delusion there is only lack of familiarity to familiar faces, leading to the delusion of familiar persons being replaced by identical impostors. In this hypothesis, the psychopathology in Cotard’s syndrome is more severe and more generalized.\textsuperscript{84,86} On the other hand, the lack of feeling of familiarity cannot completely explain the pathophysiology of delusional misidentification syndromes. Patients with brain damage of the ventromedial region of the frontal cortex also demonstrate absence of differential autonomic responsivity to familiar faces, despite the absence of delusions. The same is seen in patients suffering from pure autonomic failure. There a lack of differential autonomic responsivity to anything is seen despite the absence of delusions. Therefore, to explain delusions a second factor is needed. This factor is responsible for the failure to reject the hypothesis (eg, I’m dead as an explanation for the lack of feeling of familiarity to anything) despite the presence of (often overwhelming)
In general, no further statements can be made about M&B 2011; 2:(1). July 2011 70 www.slm-psychiatry.com
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evidence against it.82–87 Hence, for Cotard’s syndrome, a two-factor hypothesis is proposed. Here, the first factor contributes to the total lack of autonomic response to anything (as in pure autonomic failure), the second to not being able to reject the hypothesis “I’m dead.”84,86 In this hypothesis the loss of affect (first factor) is more pronounced and generalized than in Capgras patients.90 On the other hand, the difference in attributional style could also be an explanation for the different hypothesis formation in the first factor.17

The importance of the right dorsolateral prefrontal cortex (RDLPFC) for hypothesis evaluating was demonstrated with fMRI.87–88 It has also been observed that right frontal damage is commonly occurring in cases of delusional misidentifications (including Cotard’s syndrome).84

PROGNOSIS AND TREATMENT

Complete recovery may occur as spontaneously and as suddenly as its onset, even in the most severe cases.12 Enoch and Trethowan13 link the prognosis to the underlying disorder.

If the nihilistic delusions are related to an acute psycho-organic syndrome, the prognosis is good and the condition tends to resolve. If, however, it is associated with a depressive illness, it may well persist even when the other symptoms of the depressive illness have cleared. Under this circumstance, and where the condition becomes chronic, the delusional state of negation usually waxes and wanes in intensity, depending on the periodic fluctuations of the depressive disorder. When the phenomenology is part of a schizophrenic illness, it usually improves when the other symptoms respond to therapy, but it can also persist for years as part of a chronic schizophrenic condition.12

In general, no further statements can be made about prognosis from the available literature. In most publications, prognosis is not discussed. It seems prognosis can widely vary from spontaneous recovery to a very severe chronic condition. An important exclusion for this is when Cotard’s syndrome is diagnosed under the age of 25 years. In these cases, there seems to be an association with bipolar classification system. It has to be diagnosed as part of an underlying disorder. Also treatment is guided by this diagnosis. Although Cotard’s syndrome is more like a symptom of its underlying condition, in our opinion recognition of this phenomenological entity remains important. Its very specific presentation, in spite of the extensive list of etiologies indicating a shared pathological pathway, is intriguing. In the management of these patients, a better

DISCUSSION

Despite that Cotard’s syndrome was first described more than a century ago, literature on this topic remains restricted to case reports. Although the syndrome is rare, more larger scale research is needed to further clarify the pathophysiological underpinnings of the disease and its relation to other delusions of misidentification such as Capgras syndrome. Promising hypotheses have been formulated but evidence-based support is lacking. To elucidate uncertainties regarding epidemiology, course, associated diseases, treatment options, and prognosis, a careful registration of all cases could be of great value. In this regard, recognition of this condition is essential. The restriction of publications to case reports is a potential pitfall. Sometimes general conclusions on course, pathophysiology, or treatment are made, based on one or a few cases. On this topic, the literature has to be read carefully.

The syndrome as such is not catalogued in our current classification system. It has to be diagnosed as part of an underlying disorder. Also treatment is guided by this diagnosis. Although Cotard’s syndrome is more like a symptom of its underlying condition, in our opinion recognition of this phenomenological entity remains important. Its very specific presentation, in spite of the extensive list of etiologies indicating a shared pathological pathway, is intriguing. In the management of these patients, a better
understanding of the psychopathology and its neuropsychological mechanisms can be of great value. Specific safety measures can also be required due to the dramatic symptomatology.

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