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COTARD'S SYNDROME IN DEPRESSION - A LITERATURE REVIEW

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ABSTRACT

Aim: Cotard's syndrome is a very rare mental dysfunction which can occur in certain situations. Medical literature describes a multitude of reasons that may turn out to be the cause of this syndrome, like schizophrenia, psychosis or depression. Out of those disorders, depression is the most common, yet it is not often associated with delusional psychoses, which can cause misdiagnosis. Thus, our review focuses solely on Cotard's syndrome in relation to depression as opposed to other reviews that describe all causes of Cotard's syndrome.

Methods: The research methodology involved conducting a thorough examination of scientific articles accessible through databases like PubMed and Google Scholar. The team reviewed content from 1995 to 2024 with a particular focus on the most recent developments. In the study, older scientific texts were also utilized to present the historical context. By systematically organizing and validating the content, 48 of the most dependable publications were singled out as the primary basis for the study.

Results: According to the most dependable sources, Cotard syndrome in most patients occurs in conditions associated with depression.

Conclusion: The search for the sources of this syndrome may provide crucial insights, as depending on the primary accompanying condition to Cotard's syndrome, the treatment course may vary. The knowledge of the underlying medical condition from which Cotard's syndrome originates is crucial in planning treatment and determining the length of recovery. It also affects the diagnostic capabilities of medical staff and the speed at which a diagnosis is made. Additionally, it significantly influences the prognosis and frequency of hospitalization. Therefore, understanding the cause of Cotard's syndrome is much more important than simply identifying the occurrence of the syndrome itself. The prognosis also significantly varies depending on the likely cause. In this review we will look for these concerns when the primary accompanying condition is depression.

Keywords: Cotard’s Syndrome, depression, Cotard’s delusion, nihilistic delusion

INTRODUCTION

Examining syndromes characterized by isolated delusions, such as Cotard’s syndrome, could offer valuable insights into the underlying pathophysiological and neuropsychological mechanisms of these and other disorders characterized by delusional symptoms. Therefore, the study of phenomenology remains essential for advancing our understanding of brain function in the future.

The first observation described by Jules Cotard outlines the main six characteristics that can occur in this syndrome. It consists of anxious melancholia, a strong belief of being dead, suicidal behavior, lack of pain or sensation, hypochondria, and a delusional conviction of decomposing parts of a body [11] and it is considered as classical symptoms of this disease.

Certain authors have linked Cotard syndrome only with the belief of being deceased, although this aspect is not integral to the syndrome. Based on historical statistical analysis, denial of self-existence is observed in just 69% of cases, while paradoxically, 55% of patients may experience delusions of immortality [36].

Analyses show that nearly 89% of cases of Cotard’s Syndrome were associated with depression, making depression one of the most relevant diagnoses that could aid in diagnosing the aforementioned syndrome [2]. Stating depression in a patient with atypical symptoms can help expedite the diagnosis of such a rare condition as Cotard's syndrome. A study case shows that patients diagnosed with Cotard's Syndrome have a higher likelihood of experiencing depression than the general population [30]. Cotard patients commonly demonstrate an internal attributional style linked with depression [21].

DEFINITION AND HISTORY

Woman X claims that she lacks multiple organs such as brain, nerves, stomach, intestines, and body parts like chest. The sole remnants within her comprised solely of skin and bones which were already decomposing. Additionally she asserts that she has no soul and rejects the existence of both God and the Devil. Following that logic she has no desire to eat or drink. Surprisingly, she firmly believes that she cannot die like everyone else; someone must set her on fire to cease her existence permanently. [9] This is the first description of a syndrome, which at the time was unknown, that scientist named Jules Cotard examined.

The very first medical practitioner to take an interest in this topic and make observations was Jules Cotard, French neurologist mentioned above. He called it “le délire de négation” ("nihilistic delusion")[33]. The translation might be misleading because the French term “délire” is much more meaningful than English “delusion”. The term “délire” includes simultaneously emotional and intellectual sphere as well as volitional symptoms, which makes English phrase much less potent, therefore authors prefer using the eponym “Cotard’s Syndrome” [36].

The patient suffering from presented syndrome described by Cotard has a delusional psychosis in which he/she strongly believes that he is dead or decomposing [40]. Described syndrome is very rare and sometimes hard to diagnose [12]. According to Cotard, it may occur in severe melancholia, sometimes accompanied by profound hypochondria [40].

In The 100 Cases study authors have identified three subtypes of Cotard's syndrome:

1. Psychotic depression, which includes patients with melancholia and nihilistic delusions.
2. Cotard type 1, consisting of pure forms of nihilistic delusions without affective symptoms.
3. Cotard type 2, characterized by a mixed group of symptoms including anxiety, depression, and auditory hallucinations [2].

ETIOLOGY

Cotard believed that the main reason for developing this syndrome is in the patient's personality [9]. It has been proven that patients with internal attributional style in paranoid or depression state are more likely to suffer from Cotard’s Syndrome. Cotard’s patients more often have a style of internal attribution associated with depression. Therefore those patients connect their condition with changes inside their bodies. The emotional deficiency in Cotard cases could be widespread, stemming from the broad impact of depression's neurochemical substrate. Individuals with suppressed overall emotional reactions might justify their lack of response by claiming they lack physical existence.

Several authors have proposed that the most thorough explanation of monothematic delusions like Cotard's delusion involves factors at two levels: the experiential and the inferential [10], [43]. Two-factor models therefore introduce an additional explanatory factor to explain how perceptual anomalies result in the

acceptance of delusional beliefs. Recognizing these factors may aid in diagnosis, yet their presence does not always lead to the occurrence of psychosis [27].

A one-factor theory has also been proposed. It could be interpreted as "global disconnection" - all sensory areas are disconnected from the limbic system [35]. The distinction between Capgras and Cotard delusions cannot be solely attributed to different styles of attribution applied to a similar affective deficit. The Cotard delusion, particularly in severe cases, arises as a rationalization of a sense of disconnection from one's body due to profound depression, which results in a widespread suppression of emotions. Conversely, in Capgras cases, the affective deficit is more specific, occurring primarily in relation to familiar individuals [21].

In Cotard cases, the delusion arises from a deficit in reasoning and internalizing attributional style [6]. It was tested in a 2007 McKay & Cipolotti study. In some cases, it has been associated with difficulties in recognizing faces [30]. The same disorder can lead to the occurrence of another syndrome - Capgras syndrome [42], [44]. Disruptions in the emotional aspect of visual recognition can occur in both Cotard and Capgras cases. However, Capgras patients tend to interpret these experiences with a paranoid and projective attributional style, while Cotard patients interpret them with a depressive and introjective attributional style. In other words, a patient with Capgras syndrome will believe that since they do not recognize the face of their loved one, they must be dealing with a substituted impostor. Conversely, a patient with Cotard syndrome, who does not recognize the face of their loved one, will believe that something is wrong with themselves—they are dead [30].

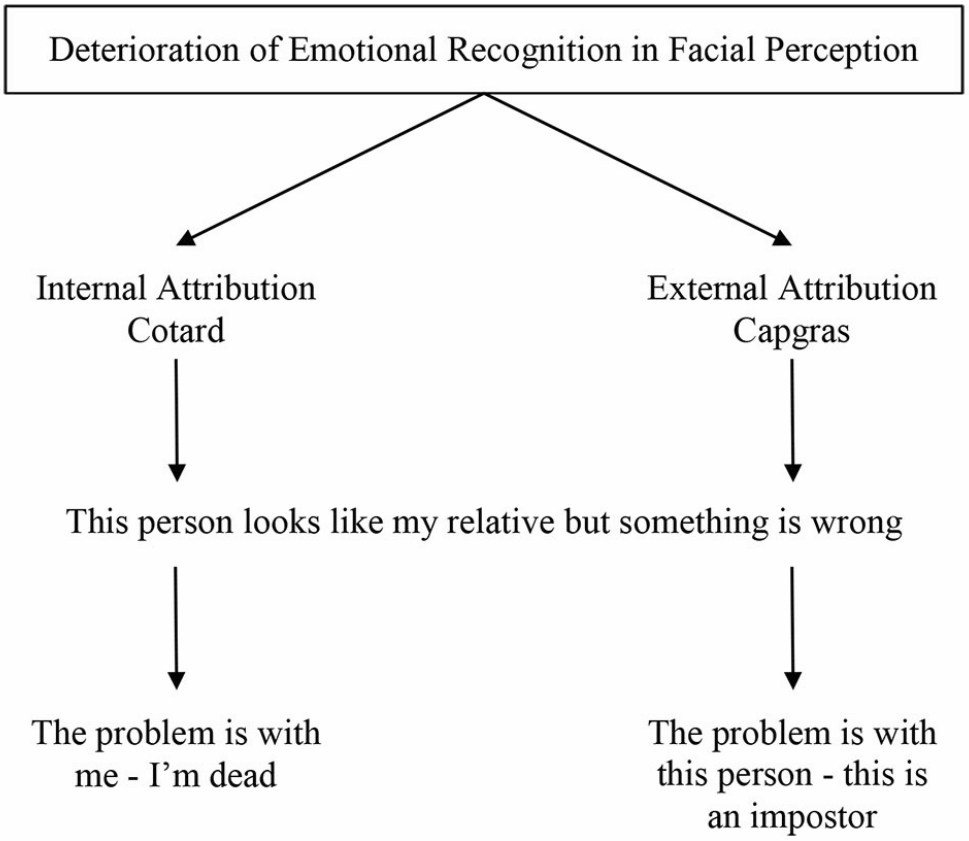

Fig. 1. Based on Young and colleagues [44].

It was proposed that the neurochemical basis of psychotic depression leads to a widespread loss of emotions, including the familiarity of local affect. In this scenario, there are two potential explanations:

(a) According to the Attribution Hypothesis, the overall deficit in emotions is explained through normal attributional processes.

(b) The Deficit Hypothesis suggests that abnormal reasoning processes are employed to rationalize the global deficit in emotions. The delusions persisting despite mounting contradictory evidence must involve deficits in reasoning in addition to perceptual malfunction and attributional biases [21].

It may also occur as a result of organic injury [4]. There are some cases that prove that this type of injury, which can lead to Cotard's Syndrome, may occur during the perinatal period. In studies involving patients with brain injury, changes are observed in NMR in several parts of the brain such as nondominant frontal, temporal and parietal lobes [41]. Cotard's Syndrome may have been even caused by ischemic stroke. The

patient in the cited study had a stroke localized in the right temporoparietal region, which led to a delusional disorder manifesting as the simultaneous occurrence of Cotard and Capgras syndromes [38].

IMAGING RESULTS

The majority of neuroimaging data indicate no significant structural alterations in the brain in Cotard's syndrome [22], [14].

A Magnetic Resonance Imaging (MRI) scan can reveal abnormalities in a patient's brain [30]. There is a case study in which MRI presented cerebral atrophy with mild subdural effusion [22].

A case report involving a 43-year-old male with Cotard syndrome utilized single photon emission computed tomography (SPECT) to investigate regional cerebral blood flow (rCBF) and dopamine D receptor binding before and after successful treatment. No changes were observed in regional cerebral blood flow, as measured by Tc-HMPAO-SPECT. However, I-IBZM-SPECT analysis revealed decreased binding of D receptors in the striatum, which further decreased after treatment [37].

EPIDEMIOLOGY

1. sex

Women appear to be more vulnerable than men [15].

2. age

The delusion occurs in children [31], in adolescents [13], [39] and in the elderly [2].

The probability of experiencing Cotard's Syndrome seems to rise as individuals get older [2], [14]. The analysis of 100 cases revealed an average age of 56 years [2], another study revealed age of 47.7 [8] . Cotard's syndrome in teenagers and young adults is linked to a heightened likelihood of developing bipolar disorder [8].

CLASSIFICATION

Cotard’s Syndrome isn’t specifically defined in the currently effective classification system (DSM-5, ICD-10, ICD-11) as an independent medical condition. Symptoms associated with this syndrome may be classified under different categories, such as delusional disorders (e.g., ICD-10: F22, ICD-11: 6A24, DSM-5: 297.1) or other mood affective disorders (e.g., ICD-10: F30-F39, ICD-11: 6A60, 6A61, 6A62, 6A6Y, 6A70, 6A71, 6A72, 6A7Y; DSM-5: eg. 296). [18], [19].

COMORBIDITY

Cotard’s delusion often co-occur with other mental dysfunction. Most common are bipolar depression and psychotic disorder [12]. There are also additional uncommon mental conditions that occur with that syndrome such as Lycanthropy [23], mental retardation [24], postictal depression [31], hydrophobia [32], Capgras delusion (this is a syndrome in which a person believes that their loved ones have been replaced by unfamiliar impostors.) [15], voluntary starvation [22].

The process of development is not fully known but there are some hypotheses. Several authors suggests that Cotard’s syndrome can have an organic origin, caused by brain injury [4], ischemic stroke [38], cortex atrophy [7], subdural hemorrhage [34], arteriovenous malformations [20], multiple sclerosis [20], Parkinson’s disease [36] typhoid fever [5], migraine [3], tuberculosis infection in an HIV patient [16] and much more. In other cases this syndrome has been proven to have a purely psychological basis.

TREATMENT OPTIONS

Patients diagnosed with Cotard's Syndrome should be treated for the primary disease [11]. Most common treatment in depressive disorder is consisted of antidepressant drugs such as selective serotonin reuptake inhibitors (SSRIs) [17], serotonin-norepinephrine reuptake inhibitors (SNRIs) [26], tricyclic antidepressants (TCAs), and others. Doctors can also use antipsychotic drugs like olanzapine with success when needed [22].

Depression could be treated successfully by electroconvulsive therapy (ECT) so Cotard's syndrome can also be treated this way [23], [29], [28], [41]. In some study cases, it is believed that combining pharmacology with electroconvulsive therapy (ECT) could provide the most impactful effect [12]. The latest case report highlights the significance of evaluating anti-recoverin antibodies by clinicians and considering encephalitis as a potential differential diagnosis when encountering sudden onset neuropsychiatric symptoms, such as

Cotard and Capgras delusions. If immunotherapy proves ineffective, electroconvulsive therapy (ECT) may be considered as the subsequent treatment option for this condition [1].

It is also reported that augmentation therapy with bromocriptine has been adjusted with good effect [25]. When the primary condition is schizophrenia, standard medications for this condition can be successfully used.

CONCLUSION

While Cotard's syndrome does not neatly fit into our existing classification system and is primarily diagnosed based on observed phenomena, it is believed that it may represent various disorders, including somatic, neurological, and psychiatric conditions. The commonalities observed across these cases suggest that there may be a shared psychopathological pathway contributing to the development of these delusions. Nihilistic delusions related to the body and existence were identified as the most frequent phenomenological features of Cotard's syndrome.

In the reviewed scientific articles, depression is the most common diagnosis among patients with the condition and, as such, in almost 9 out of 10 patients Cotard's syndrome can be attributed to depression. The treatment for Cotard's syndrome should be based on the treatment for the primary disease. With depression being the most common primary disease in Cotard's syndrome patients, the most common treatments for Cotard's syndrome are treatments for the depression itself.

The lack of classification of Cotard's syndrome and common association with psychotic disorders like schizophrenia and psychosis rather than depression, might cause misdiagnosis followed by the mistreatment, which can lead to unnecessary prolonged pharmacotherapy.

As such, it is crucial to diagnose the underlying cause of Cotard's syndrome and treat it accordingly.

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