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What Are the Current and Developing Treatments for Cotard's Syndrome, Alice in Wonderland Syndrome, and Catatonic Schizophrenia?

Anuva Ghosh

New York University, New York, NY, USA
Email: anuvag05@gmail.com

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Abstract

Purpose: Cotard's syndrome, Alice in Wonderland Syndrome, and Catatonia are all rare psychiatric disorders that have relatively little research regarding their treatments. The aim of this article is to highlight any gaps in knowledge regarding represented demographics in these treatment studies, and to discuss the current and upcoming treatment options. **Background:** This literature review explores under-researched psychiatric conditions: Cotard's syndrome, Alice in Wonderland syndrome, and Catatonic Schizophrenia. Understanding psychiatric disorders requires basic knowledge of brain anatomy. These conditions are often result of or associated with neurological issues, such as migraines or tumors. The brain has eight lobes, two of four kinds: frontal, parietal, occipital, and temporal lobes, which all govern different functions and abilities. Frontal lobes control judgment, decision-making, personality traits, and fine motor movements. Parietal lobes interpret pain and temperature, occipital lobes handle visual stimuli, and temporal lobes enable hearing. The pre-frontal cortex is associated with high intelligence, psychotic traits, and psychosis. The Broca's Area in the frontal lobes controls expressive language. These areas and divisions of the brain contribute to the complexity of the psychiatric disorders discussed in this review. **Introduction:** Cotard's syndrome is a psychiatric disorder characterized by delusions of being dead or not having certain limbs or organs. It is believed that there is a disconnect between their fusiform face area and the amygdala, causing a lack of familiarity between one's mind and body. Alice in Wonderland Syndrome (AIWS) is another psychiatric disorder which is characterized by visual hallucinations, such as distorted perceptions of color, size, distance, and speed. The most common symptoms include micropsia and macropsia. Catatonia/Catatonic

Schizophrenia is an uncommon type of schizophrenia. This type of schizophrenia is characterized by motor rigidity, verbal rigidity, the flat effect, psychomotor retardation, waxy flexibility, and overall negative symptoms. Thus, these people may come off as emotionally detached, and able to stay frozen in odd positions for periods on end. **Treatments and Results:** Cotard's syndrome seemed to be most effectively treated by ECT (electroconvulsive therapy). Alice in Wonderland Syndrome (AIWS) had the highest positive responses to treatment by Valproate (an anti-epileptic drug), as well as intervention to treat the associated neurological conditions they had. Catatonia/Catatonic Schizophrenia seemed to be most effectively treated with a combination of benzodiazepines and ECT. **Discussion and Demographics:** In all 3 disorders, the Latino and African communities were underrepresented. There also seemed to be an underrepresentation of men in Cotard's syndrome, and of women in Alice in Wonderland Syndrome. Japan and India seemed to have the highest density of treatment studies in all 3 disorders.

Keywords

Component, Formatting, Style, Styling, Alice in Wonderland Syndrome, Cotard's Syndrome, Cotard's Delusion, AIWS, Catatonia, Catatonic Schizophrenia, Schizophrenia, Psychiatric medication, Rare Disorders, Psychiatry

1. Background and Introduction

This is a scientific literature review of 3 psychiatric conditions that have yet to have extensive research done on them and their treatment options. These conditions are Cotard's syndrome, Alice in Wonderland syndrome, and Catatonic Schizophrenia (otherwise known as Catatonia). To begin the systematic understanding of these disorders, one must have a clear understanding of what a psychiatric condition is and have an overview of basic brain anatomy. A psychiatric condition or disorder is a problem or multitude of problems that affect a person's thoughts, behavior, or mood [1]. Psychiatric conditions are typically diagnosed after biological or medical causes have been eliminated as possibilities for these changes in thoughts, behaviors, and mood. However, it is often seen that some rare psychiatric conditions can accompany or be side effects of certain neurological disorders, such as those that cause changes in brain anatomy. These can include migraines, brain tumors, and severe headaches that can cause such associated psychiatric conditions to develop [1]. As a brief overview of brain anatomy, the brain is divided into 8 lobes, or 4 types of lobes divided into each of the left and right hemispheres [2] (**Figure 1**). These lobes include the frontal lobes, parietal lobes, temporal lobes, and occipital lobes. The frontal lobes are responsible for judgment and decision-making. They are arguably the lobes that give us the highest functioning and what make humans so much more

capable of intelligence and higher cognitive functions than other mammals [3]. The frontal lobes also hold innate personality traits, critical analysis capabilities, speech/expressive language, and some fine motor movements. It has also been discovered that there is a correlation between the pre-frontal cortex (a region of the frontal lobes) and being either extremely high-functioning and intelligent or being psychotic [4]. Another region of the frontal lobes, called the Broca's Area, is responsible for expressive language, such as speech. The next regions of the brain that are of interest are the parietal lobes. The parietal lobes provide the tactile feedback associated with sensory functions. These lobes allow us to interpret pain, temperature, and touch. Thus, people who have damaged parietal lobes may not be able to interpret, or at least not interpret correctly, pain and temperature changes [5]. Next, we have the occipital lobes. The occipital lobes interpret visual stimuli. Light images, which hit the eye, are refracted in the retina, are relayed to a brain structure called the thalamus, and then get relayed to the occipital lobes for us to see. Images on the left side of the visual field are transmitted to the right occipital lobe while images on the right side of the visual field are transmitted to the left occipital lobe [4]. The occipital lobes also have specialized neurons called feature detectors, which allow us to see fine lines and details in images. Finally, the temporal lobes are the structures in the brain that allow us to hear. When sounds hit the eardrum, the vibrations are transmitted to the temporal lobe. Sounds in the right ear are transmitted to the left temporal lobe while sounds in the left ear are transmitted to the right temporal lobe [3]. All of these lobes, the frontal, parietal, occipital, and temporal, are all part of the vast brain structure called the cerebrum.

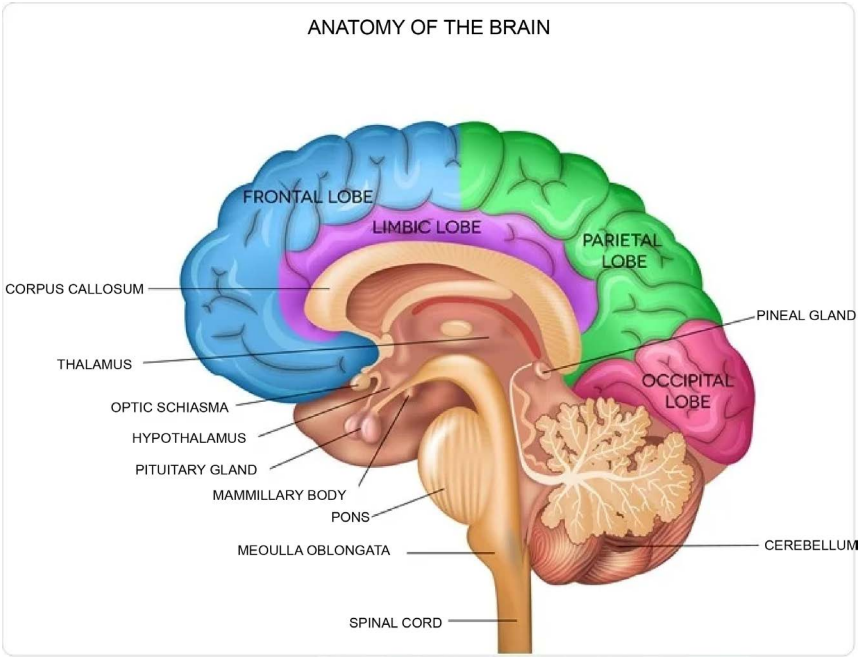

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Figure 1. Anatomy of the Brain.

There are other structures in the brain that are also important to consider to be able to understand psychiatric conditions. These structures include the cerebellum, the brainstem (and the structures that make it up), and the cerebrum [4]. The cerebellum is the 'mini brain' which is associated with coordinated muscle movements and balance. It is mainly responsible for gross motor movements, meaning the movement of larger organs that do not require too much precision or dexterity. The frontal lobes are responsible for fine motor movements which do require dexterity, such as moving your fingers. The brainstem is the most vital part of our central nervous system. It is responsible for the autonomic functions that keep us alive. There are 3 main parts to the brainstem; the medulla oblongata, the pons, the midbrain, and the thalamus [4]. The medulla oblongata is responsible for controlling autonomic activities like breathing, heartbeat, swallowing, metabolic activities, and temperature control. Since the medulla is so vital, damaging it could potentially kill someone instantaneously. The pons is responsible for controlling facial expressions and movements, as well as controlling the sleep-wake cycle. The midbrain is responsible for relaying information for visual and auditory processing. The thalamus is responsible for relaying all incoming information to their respective destinations in the brain. All sensory stimuli, with an exception for olfaction (smell), pass through the thalamus before going to their respective lobes. Olfaction is different in that its sensation goes directly to the olfactory bulb in the brain rather than passing through the thalamus [4].

Furthermore, it is important to understand the basics of how neurons communicate with each other. There are 5 main parts to a neuron; the dendrites, the cell body (soma), the axons, the myelin sheath, and the terminal buttons [5] (**Figure 2**). The dendrites are the bushy branched out extensions of the neuron that integrate incoming messages/signals into the neuron. The cell body/soma is the part of the neuron that holds the nucleus, acting as the cell's life support center. The axons form the branched out extension of the neuron that passes action potentials from the neuron. The action potential is a chemical-electrical process that is activated once enough neurotransmitters have binded to the dendrites of the neuron, and is an 'all-or-nothing' response. The myelin sheath is the fatty tissue layer that segmentally encases the axons, meant to provide insulation and faster transmission of action potentials. It is important to note that the degradation of the myelin sheath is correlated with the onset of the debilitating disorder, multiple sclerosis [5]. Finally, the terminal buttons are the extensions of the axon that hold the neurotransmitters to be sent to the next neuron across a synapse (a junction between neurons). Once the action potential has passed through the axon and down to the terminal buttons, it releases certain neurotransmitters to be passed along and buildup in the dendrites of the next neuron, initiating another action potential in that neuron [5]. This encapsulates the process of how neurons communicate with each other.

Finally, it is very important to note the different types of drugs used to treat

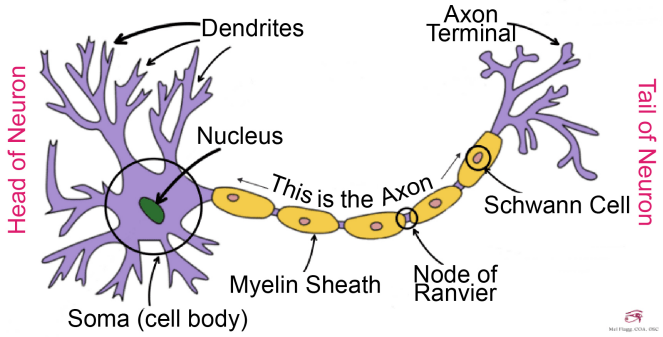

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Figure 2. Anatomy of a Neuron.

psychiatric disorders. These major drug groups include antidepressants, anti-anxiety medications, antipsychotics, depressants, stimulants, and hallucinogens. Antidepressants are widely known as SSRI's, one of the major types of antidepressants. SSRI's stand for selective serotonin reuptake inhibitors [6]. Anti-anxiety medications are often called benzodiazepines [7]. The most common benzodiazepines are lorazepam and diazepam. Antipsychotic medications most commonly include Quetiapine, Aripiprazole, Risperidone, and Olanzapine [8]. Stimulant drugs are meant to speed up body functions and excite neural activity; the most common and widely used stimulant being caffeine [9]. The other is widely known stimulant class being amphetamines. Depressants are meant to slow down body functions and reduce neural activity, and the most common ones are barbiturates and opiates [9]. Hallucinogens are psychedelic drugs that distort perceptions and provide fake sensory images in the absence of them [10]. The most common hallucinogens are LSD, Ecstasy (MDMA), and THC (in Marijuana). Other forms of treatment of psychiatric disorders include ECT (electroconvulsive therapy), rTMS (rapid transcranial magnetic stimulation), and common talk therapies such as cognitive behavioral therapy, all of which will be brought up frequently in this review.

Now, a brief introduction of the 3 psychiatric disorders is also required to understand the basic signs, symptoms, and causes of them.

1.1. Cotard's Syndrome

Cotard's syndrome is a psychotic disorder in which one experiences delusions that their limbs and/or organs have fallen off/out or have completely disappeared [10]. They also may claim that they are dead, hence why it is also called 'Walking Corpse syndrome'. The signs of this may be that someone is claiming that they have lost their limbs or that their organs do not exist, when, in fact, they are all intact and unharmed. They may also be very paranoid, depressed, and anxious. The causes of this syndrome are unknown, but there is a theory that a part of the brain called the fusiform face area loses connection with the amygdala, causing a loss of recognition when someone with this syndrome looks

in the mirror [10]. This leads to the delusion that they are dead or are missing parts of their body.

1.2. Alice in Wonderland Syndrome (AIWS)

Alice in Wonderland Syndrome (AIWS) is characterized by visual hallucinations and interpreting distortions in the visual field [11]. The symptoms of this disorder are incorrect perception of speed, distance, and most commonly, size. People with this disorder may perceive objects or people in their visual field to be larger or smaller than they really are. They may even perceive different 'auras' to them [11]. There is no known direct cause for this disorder, however, there is a large correlation between AIWS and other neurological conditions, such as migraines, brain tumors, and severe headaches, as will be examined later in this review.

1.3. Catatonic Schizophrenia/Catatonia

Catatonic Schizophrenia/Catatonia is characterized by its negative symptoms, such as waxy flexibility, motor rigidity, verbal rigidity, and more [12]. These people are known to stay frozen in odd positions for hours or days on end. They also tend to have insomnia, anxiety, and depression associated with it. The causes of this disorder are unknown, but like all categories of schizophrenia, there is data that supports the idea of hereditary/genetic causes of this disorder [12].

I am choosing to review these psychiatric conditions because of their uniqueness and rarity. Since they are so rare, there are very few studies divulging into the treatment options for these disorders. Thus, I wish to expand their knowledge base.

1.4. Aim of Review

The aim of this scientific literature review is to provide more information about current and upcoming treatments for marginalized, rare psychiatric disorders. Since these disorders are so infrequently documented and diagnosed, they often do not have many studies done on them and have a smaller basic knowledge basis. So, it is important to provide accurate information about them and their treatments. Cotard's syndrome was first documented in 1880 by Jules Cotard. Even though this disorder, as well as Alice in Wonderland Syndrome and Catatonic Schizophrenia, was discovered so long ago, there is still little research done on them. They are also often treated as side effects of other neurological and psychiatric disorders, so they are often unnoticed or unmentioned. Thus, the aim of this review is to treat these conditions as their own disorders and discuss their treatments, and to fill the gap of information. These treatments include medications, therapies, lifestyle changes, and surgical intervention.

1.5. Cotard's Syndrome

In Cotard's syndrome, there seems to be a lack of African and Latino overall

populations present in research studies. The countries of the studies collected include Japan, the United States, the United Kingdom, and India. Thus, there are quite a few gaps of information present based on this demographic. Furthermore, there seems to be more research and case studies done on women with Cotard's syndrome than men. Thus, Africans, Latinos, and men seem to be underrepresented demographics in studies of Cotard's syndrome.

1.6. Alice in Wonderland Syndrome

In Alice in Wonderland Syndrome, it is seen that this syndrome is especially discussed only as a side effect of other neurological conditions, such as migraines, tumors, and cluster headaches. Furthermore, there seems to be a lack of women represented in these studies. In the studies chosen, the countries of origin included Japan, Turkey, Italy, and Egypt. Thus, we are missing demographic information from Africans, Latinos, and Europeans. Furthermore, it is important to note that the majority of Asian studies conducted on all 3 disorders are from Japan (and occasionally India). Thus, a wide majority of European people and Asians are also underrepresented in these studies.

1.7. Catatonia/Catatonic Schizophrenia

In Catatonic Schizophrenia/Catatonia, there seems to be a large amount of research done in Japan. Over half of the research studies chosen are from Japan. Here, once again, we see an underrepresentation of Africans, Latinos, and Europeans. The countries of origin of the articles done on this disorder are the United States, Japan, India, and Turkey. Thus, we can see Japan taking the lead in researching all 3 of the disorders of interest for this scientific literature review. There does not seem to be a significant gender inequality in research done on Catatonic Schizophrenia/Catatonia (Table 1).

2. Research Question

What are the current and developing treatments for Cotard's Syndrome, Alice in Wonderland Syndrome, and Catatonic Schizophrenia?

2.1. Inclusion and Exclusion Criteria

Ctard's Syndrome (Databases: PubMed and Google Scholar):

I chose the same databases (PubMed and Google Scholar) for researching and finding articles of Alice in Wonderland Syndrome. The searches included were "Alice in Wonderland Syndrome treatment" and "AIWS treatment" (Table 2). The articles were again, further narrowed based on their inclusion of discussion sections of the treatment(s) used and the patient responses to the treatments, as well as if alternatives were offered. These studies mainly included case studies, testing out drugs (clinical trials) to see if they alleviate symptoms of Alice in Wonderland Syndrome. Furthermore, the results were limited to having been published from 2010 to 2023, as were the parameters for Cotard's Syndrome.

Table 1. Catatonic Schizophrenia.

Inclusion Criteria	Exclusion Criteria
Searches: Cotard's Syndrome treatment, Death Delusion treatment, Cotard's Delusion treatment, Cotard's syndrome, and Cotard's Delusion	Clinical trials not done
In-depth discussion section of treatment	No in-depth discussion of treatment
Effects of treatment on individual	No effects of treatment on individual discussed
Dosages of treatments mentioned	No dosages of treatments mentioned
Patient responses to treatment	No patient responses to treatment recorded.
Clinical trials, meta-analyses, randomized control trials, books, and documents, and reviews	Systematic reviews
Published within 2010-2023	Published before 2010
Only humans (in clinical trials)	Only animals (in clinical trials)
Article language in English	Article language not in English
Free-full text available	

Table 2. Alice in Wonderland Syndrome treatment and AIWS treatment.

Inclusion Criteria	Exclusion Criteria
Searches: Alice in Wonderland Syndrome treatment and AIWS treatment	Clinical trials not done
In-depth discussion section of treatment	No in-depth discussion of treatment
Effects of treatment on individual	No effects of treatment on individual discussed
Dosages of treatments mentioned	No dosages of treatments mentioned
Patient responses to treatment	No patient responses to treatment recorded.
Clinical trials, meta-analyses, randomized control trials, books, and documents, and reviews	Systematic reviews
Published within 2010-2023	Published before 2010
Only humans (in clinical trials)	Only animals (in clinical trials)
Article language in English	Article language not in English
Free-full text available	

The filters, once again, excluded any other systematic reviews, articles in any language other than English (unless translated to English), and studies only involving humans (no trials done on animals). Other than this, the parameters also only fit free articles (which is why PubMed and Google Scholar were the databases of interest).

2.2. Alice in Wonderland Syndrome (AIWS) (Databases: PubMed and Google Scholar)

I chose the same databases (PubMed and Google Scholar) for researching and finding articles of Alice in Wonderland Syndrome (Table 3). The searches included were "Alice in Wonderland Syndrome treatment" and "AIWS treatment." The articles were again, further narrowed based on their inclusion of discussion sections of the treatment(s) used and the patient responses to the treatments, as well as if alternatives were offered. These studies mainly included case studies, testing out drugs (clinical trials) to see if they alleviate symptoms of Alice in Wonderland Syndrome. Furthermore, the results were limited to having been published from 2010 to 2023, as were the parameters for Cotard's Syndrome (Table 4 and Table 5). The filters, once again, excluded any other systematic reviews, articles in any language other than English (unless translated to English), and studies only involving humans (no trials done on animals). Other than this, the parameters also only fit free articles (which is why PubMed and Google Scholar were the databases of interest).

2.3. Catatonic Schizophrenia (Catatonia) (Databases: PubMed and Google Scholar)

I chose the same databases for research and inclusion of articles on Catatonic Schizophrenia/Catatonia (PubMed and Google Scholar (Table 6)). The searches included were "Catatonic Schizophrenia treatment" and "Catatonia treatment." The articles were narrowed based on their inclusion of discussion sections of the treatment(s) used on the patient(s) and the responses to it. Once again, this includes any alternatives or new testing drugs (clinical trials) to see if people respond to such treatments. Furthermore, the results were limited to have been published from 2011 to 2023. This is slightly different from the other disorders, which have been published since 2010. The Catatonia articles were meant to be

Table 3. Wonderland Syndrome.

Inclusion Criteria	Exclusion Criteria
Searches: Catatonic Schizophrenia treatment and Catatonia treatment	Clinical trials not done
In-depth discussion section of treatment	No in-depth discussion of treatment
Effects of treatment on individual	No effects of treatment on individual discussed
Dosages of treatments mentioned	No dosages of treatments mentioned
Patient responses to treatment	No patient responses to treatment recorded.
Clinical trials, meta-analyses, randomized control trials, books, and documents, and reviews	Systematic reviews
Published within 2010-2023	Published before 2010
Only humans (in clinical trials)	Only animals (in clinical trials)
Article language in English	Article language not in English
Free-full text available	Only abstract available

Table 4. Cotard's Syndrome.

Study	Study design	Sample Size	Assessment Time	Outcome Measures/ Instruments	Signs & Symptoms	Results	Limitations	Country
Kobayashi *et al.*, 2012 [2]	Longitudinal Case study	n = 1 - 74 year old woman with cotard's syndrome, depression, and Frontotemporal (FTD) dementia - Previous 2 years of pharmacotherapy	1 - 2 years	Observed, cognitive assessments, HDS-R scale (Dementia scale), MMSE (mini mental state examination), Brain CT scan Brain MRI Three-dimensional stereotactic surface projections (SPECT), ECT (treatment)	Atypical and nihilistic behavior Motor rigidity limited word/verbal expression Loss of appetite/anorexia Claimed that she did not have her intestines, stomach, lungs, and even claimed that she is dead	The patient was given around a total of 18 ECT sessions which resulted in fluctuated mental condition, and overall her delusions, sluggishness, slowness, appetite, and psychotic symptoms (she did not claim any missing organs) improved. But then they deteriorated again, but the patient's overall physical and mental state improved	Patient had FTD Dementia which is very specific, very confused about which symptoms were existing before or what symptoms were side effects of a disease (blurred lines between the symptoms of her diseases) Relationship unclear Small sample size (1), so the results of the study may be biased and cannot be generalized	Japan
Mughal, Menezes, 2013 [13]	Longitudinal study	n = 1 - 59 year old caucasian woman, history of depression with somatic symptoms, experienced loss of mobility, somatic symptoms resulting in suicidal ideals and complaints of pain without a definitive biological cause	About 2 months	ICD-10, ECT, Olanzapine, Antidepressants Antipsychotics pipotiazine depot injection Duloxetine MRI Verbal symptoms recorded/written SOAD	Claims of persistent back and leg pain Suicidal idealations Psychosomatic symptoms, claiming physical/biological causes of symptoms Somatisation loss of mobility (psychosomatic) Claimed she felt like a rotting corpse Claimed legs rotting and falling off	After 4 weeks of persistent antipsychotic, antidepressant, and ECT combination therapy, patient felt much happier and attended to her personal hygiene, motor disability was repaired, Nihilistic delusions resolved, Better mood No longer suicidal or homicidal	Case study, meaning the results cannot be generalized The cotard's syndrome was treated more as a symptom of the patient's psychotic depression	United Kingdom

Continued

Grover, Shah, Ghosh, 2010 [14]	Longitudinal study	n = 1 - 37 year old woman who claimed lycanthropy (converting into a pig), no history of illness, stressors possibly induced the cotard's syndrome, lives in urban area	6 weeks (1.5 months)	Venlaflaxine ECT Olanzapine International Statistical Classification of Diseases, 10th Revision hemogram, renal function tests, liver function tests, electrocardiogram, chest x-ray posterior-anterior view Modified bilateral ECT Atropine thiopental sodium Succinylcholine EEG Hamilton depression rating scale	Claimed lycanthropy (that her bones were converting to pig bones and treat she and her children overall were turning into pigs) Claimed God was punishing her for skipping prayers and religious pilgrimages Decreased sleep Anxiety Depressed mood Cried frequently Hopelessness Insomnia Poor appetite Guilt	Was treated with a combination of venlaflaxine, olanzapine, and ECT, given 6 sessions of ECT, all of her depressive, sad, and delusional and/or psychotic symptoms resolved Her depression rating scale based on the Hamilton Depression Rating Scale decreased from 30 to 3 by discharge	Case study, meaning the results can't be generalized A lot of her symptoms of guilt and depression relate to her religion and belief of herself being punished by God Many symptoms also relate to the fact that she had a suspected malignant tumor and complications Lycanthropy is a very specific symptom associated with Cotard's syndrome, not any other case studies relating to it	India
Grover, *et al.*, 2014 [15]	Double case study, longitudinal study	n = 2 1) 65 year old male, no family history of mental illness, smoked cigarettes for over 30 years, suicidal and self harming behaviors before admittance to clinic. 2) 62 year old female, bipolar affective disorder for 35 years, symptoms of psychomotor retardation, depressed mood	1) About 2 months 2) About 2 months	1) HDRS (Hamilton depression rating scale) Brain MRI Thyroid function test bilateral modified electro-convulsive treatment (ECT) Thiopentone Succinylcholine Escitalopram Olanzapine Blood tests 2) Brain MRI Blood tests Intravenous lorazepam bilateral modified ECT Thiopentone Succinlycholine BFCR scale Mood stabilizers Olanzapine Fluoxetine	1) Poor social skills Depressed mood Anhedonia Insomnia Decreased appetite Nihilism Hopelessness Feelings of sin and guilt Delusions of catastrophe, poverty, and persecution Believed he had an illness he could spread that caused cancer, reason for suicidal intent 2) Poor social skills Anxiety Depressed mood Decreased appetite Forgetfulness Psychomotor retardation Delusions of persecution and misidentification	1) Received 9 ECT treatments in total, all of his symptoms resolved completely in a matter of 7 weeks, and HSDR scale revealed score of 1 compared to initial score of 34 2) Received 8 ECT treatments and all of her depressive, catatonic, and delusional symptoms melted away during this period. Her BFCR scale (for catatonia) decreased from initially 14 to 0 by the end	Both are case reports, so they cannot be generalized to the public The first report (male) smoked for over 30 years which may have induced symptoms The second report (female) already had bipolar affective disorder, which may not be associated with Cotard's syndrome very often	India

Continued

Weiss, Santander, Torres, 2013 [16]	Longitudinal study	n = 1 - 22 year old woman who has had depression, catatonia, and Cotard's syndrome; has neuroleptic malignant syndrome as result of using Risperidone, recovered later; has leukoencephalopathy	4 months	Brain NMR ECT Haloperidol Lorazepam Risperidone Chlorpromazine Zolpidem Life support in ICU Bromocriptine Nasogastric intubation Olanzapine Lamotrigine	Trouble sleeping Decreased attention span Depressive episode Restlessness Delusions, claimed that she killed her mother, the world, saved the world, etc. Catatonia (motor rigidity)	After maintenance of ECT for 2 months, with lamotrigine and olanzapine, (4 months), she improved greatly and no longer showed delusional and psychotic symptoms. She has been euthymic and functional	The patient experienced neurological damage (leukoencephalopathy), and had an episode of neurological malignant syndrome as result of one of her prior treatments, which may have caused some of the results and cannot compare to other case studies of Cotard's syndrome It is a case study, so it cannot be generalized	United States

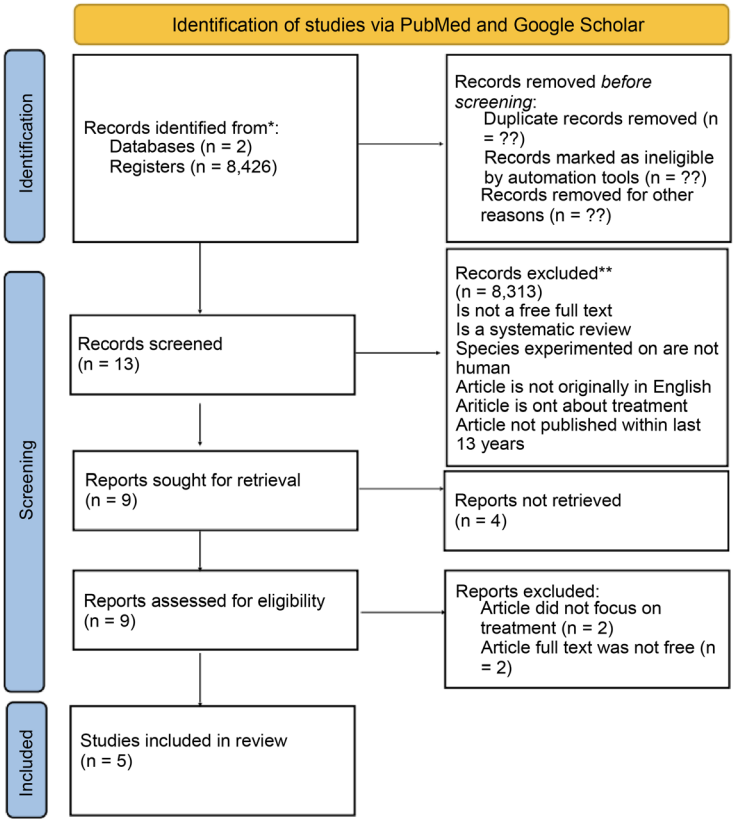

Figure 3. PRISMA Chart 2010-2023 flow diagram for case studies and clinical trial documentations of Cotard's Syndrome, Cotard's Delusion.

the same, published since 2010, but ended up not being included in the final picked papers, unlike AIWS and Cotard's syndrome. The filters were the same as before only including testing on humans (if clinical trial), excluding systematic reviews, excluding articles that were not in English (unless they were a translated English version), and only free articles (Figure 3 and Figure 4).

Table 5. Alice in Wonderland Syndrome (AIWS).

Study	Study design	Sample Size	Assessment Time	Outcome Measures/ Instruments	Signs & Symptoms	Results	Limitations	Country
Yokoyama *et al.*, 2017 [17]	Longitudinal study	n = 1 - 63 year old Japanese male who had 2 distinct episodes of depression and associated AIWS. History of type 2 diabetes mellitus and essential hypertension. No history and no family history of psychiatric disorders or drug use/abuse	4-5 years	Endocrine evaluations HIV test Brain MRI Amitriptyline Perphenazine Aripiprazole Visual Perception Test for Agnosia Mini-Mental State Examination (MMSE) Beck Depression Inventory-II (BDI-II) FDG-PET Maprotiline Duloxetine Mirtazapine SPECT SISCOM Statistical analysis	Severe, consistent, repeated periods of depression Micropsia Fatigue Altered body image Altered sense of distance and time Lost sense of speed Cannot perceive value of money No emotional weight to events Psychomotor retardation Reduced pleasure Reduced concentration	Severe, consistent, repeated periods of depression Micropsia Fatigue Altered body image Altered sense of distance and time Lost sense of speed Cannot perceive value of money No emotional weight to events Psychomotor retardation Reduced pleasure Reduced concentration After 6 months of treatment with Escitalopram, all of the depressive symptoms and associated AIWS symptoms subsided. There were also psychoeducation strategies used such as a change of environments where she usually witnessed her delusions, which also greatly contributed to the patient's recovery. The patient was also consistently reassured that the visual hallucinations and distortions in perception were not real and that they would fade over time, which may have contributed a boost of confidence which could have also contributed to recovery	Case study, so the results cannot be generalized The patient was a diabetic which could have been related to his symptoms	Japan
Tunç, Başbuğ, 2017 [18]	Longitudinal study	n = 1 - 18 year old female, university student living with her parents, history of migraine as a child which was treated from ages 7 - 14. She also had a maternal history of migraines in the family. She had no life changing stressors or neuropsychiatric history before. No medications taken and no drug use or abuse	6 months	EEG Brain MRI Blood tests (electrolyte, liver function, thyroid function, blood count) Structured Clinical Interview for DSM-IV Axis 1 Disorders Beck Anxiety Inventory Hamilton depression rating scale Alprazolam Escitalopram	The patient saw objects and people as different sizes and auras/colors than normal. Complained that her father's head was blue and enlarged and the mother being large and taller. Incorrect perceptions of distance. These symptoms occurred in episodic patterns		It is a case study so the results cannot be generalized The patient had no environmental stressors or causes of her depression and AIWS, and no abnormal neuropsychiatric background	Turkey

Continued

Uca, Kozak, 2015 [19]	Longitudinal study	n = 1 - a 35 year old male with a 4 year medical history of cluster headaches, pain attacks 3 - 5 times a day upon admittance to the hospital. No personal or family history of depression or any psychiatric illness, and no drug abuse.	3 - 4 months	General health examination Ophthalmologic examination Systemic examination Blood count test Blood pressure test EEG Serum electrolytes test Biochemistry test Brain MRI Methylprednisolone Subcutaneous sumatriptan Valproate	Had pain attacks 3 - 5 times a day lasting 0.5 - 1 hours for 3 - 4 weeks Pain localized in the left orbital and periorbital region Distorted perceptions of speed, color, and size 2 - 5 minutes before the migraines and headaches (AIWS)	After 3 months of treatment with Valproate, the patient showed clinical improvement, and complete loss of headaches (meaning a loss of associated AIWS symptoms as well). No more visual hallucinations were presented	The patient specifically had AIWS symptoms preceding his migraine attacks, and these symptoms only lasted 2 - 5 minutes It is a case study, meaning the results cannot be generalized	Türkiye
Hamed, 2010 [20]	Longitudinal study	n = 1 - 22 year old Egyptian male who had a history of migraines and abdominal colic attacks. Patient has had colic attacks for 12 years, and he has a family history of migraines and severe/ hemicranial headaches which can induce vomiting. The patient had developed hallucinations and distortions in size perception since age 17	About 8 months	Blood, urine, and stool analysis Abdominal imaging Endoscopic examinations Anti-epileptics (Valproate) Carbamazepine EEG Colchicine Brain MRI VEP and TMS Eletriptan	Intense, prolonged attacks in abdominal colic Diarrhea Nausea Abdominal flushing Pallor Decreased appetite, weight loss Teleopsia (everything looked farther and smaller) and peliopsia (larger and closer) Visual and auditory hallucinations and distortions of perception Severe headaches and migraine	Treatment has been effective, and the patient's symptoms of migraine and abdominal colic have decreased, but he will have to stay on Valproate medication for likely the rest of his life to keep it that way	The patient had abdominal colic attacks, which is rare and uncommon, meaning there are no other case studies to compare this to This is a case study, meaning the results cannot be generalized	Egypt

Continued

Mastria, *et al.*, 2018 [21]	Longitudinal study	n = 1 - 54 year old male patient who was diagnosed with temporo-parietal glioblastoma and had a history of family gliomas. He had associated AIWS symptoms due to the glioblastoma, including	About 1.5 years	EEG CT scan Brain MRI Valproate Temozolomide Radiation therapy Neurosurgery	Sensory aphasia Distorted perception of size (visual) Pelopsia Kinetopsia Headaches Decreased consciousness Nausea Photophobia	The patient had his tumor removed and was treated with chemotherapy and radiotherapy as well as valproate for his AIWS delusions - he completely went into remission from the AIWS symptoms and did not have any recurrences of it since the initial diagnosis; the glioma did return which required neurosurgery again and has been disease-free ever since	The patient is the only known case study of AIWS resulting from glioblastoma (a type of brain cancer) so it cannot be compared to other studies The study is a case study meaning the results cannot be generalized	Italy

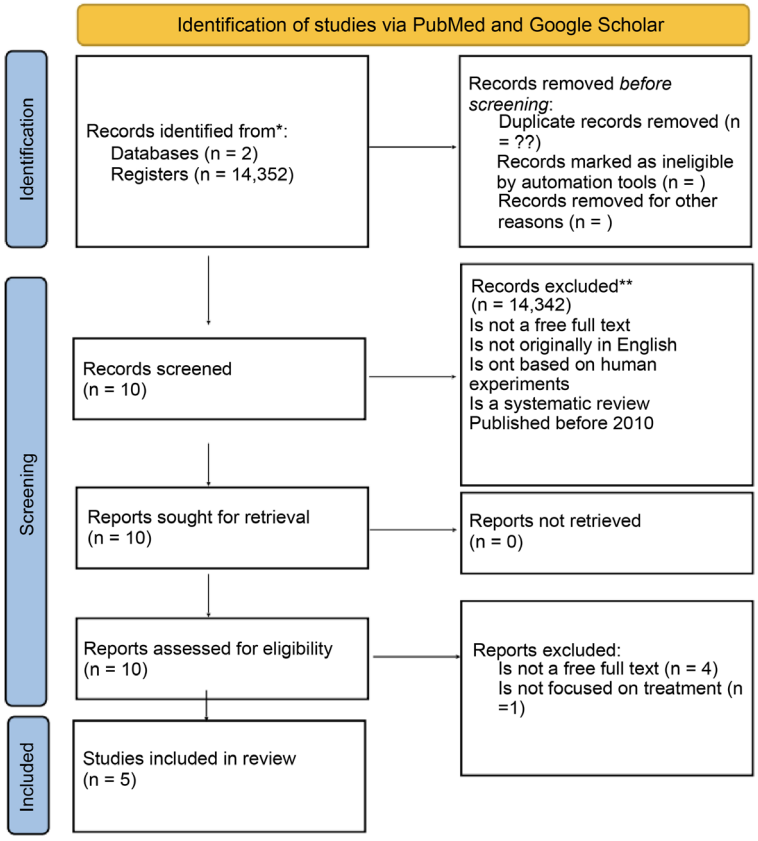

Figure 4. PRISMA 2010-2023 flow diagram for case studies and clinical trial documentations of Alice in Wonderland Syndrome, AlWS.

Table 6. Catatonia/Catatonic Schizophrenia.

Study	Study design	Sample Size	Assessment Time	Outcome Measures/ Instruments	Signs & Symptoms	Results	Limitations	Country
Chen, *et al.*, 2015 [22]	Longitudinal study	n = 1 - 30 year old male patient who has had catatonia for 10 years with no recovery from taking benzodiazepines and antipsychotic medications	Around 20 months	Positive and Negative Syndrome Scale Lab examinations Brain image studies DSM-IV 4th edition Sulpiride Lorazepam Haloperidol Lithium carbonate Fluoxetine Paroxetine	Catalepsy Mutism Posturing Mannerism Agitation Grimacing	After 2 weeks of paroxetine treatment, the patient had already begun to show decreases in catatonia symptoms and less motor rigidity. The Positive and Negative Syndrome Scale improved from 148 to 106. Showed more facial expressions No more odd postures	SSRIs are not commonly used to treat catatonia, as it is usually most effectively treated with antipsychotics and benzodiazepines This is a case study so the results cannot be generalized to the public	United States
Nomura, *et al.*, 2021 [23]	Longitudinal study	n = 1 - Asian woman in her 60's, who had a history of schizophrenia and cholelithiasis, kidney injury and high creatinine kinase levels	About 4 months	Glasgow Coma Scale Laboratory examinations (BP, heart rate, etc) Levenson diagnostic criteria Dantrolene Bromocriptine CT scan Endotracheal intubation Mechanical ventilation, intravenous rehydration cooling Continuous renal replacement therapy Amantadine L-DOPA Propofol BFCR (Bush-Francis Catatonia Rating Scale) Voriconazole L-AMB Quetiapine	Hyperthermia Verbal rigidity Muscle rigidity Elevation of creatinine kinase levels Strong rigidity in the upper and lower limbs (catatonia)	After treatment with quetiapine and propofol in combination, the patient's glucan level decreased and was already almost in remission, She was able to speak coherently and have conversations normally and was able to move easily (decreased/ nearly eliminated muscle rigidity). Eventually all symptoms of catatonia were resolved and the patient was transferred to another clinic, with minor motor disabilities	The patient had her catatonia associated with her high creatinine kinase levels and acute kidney injury, which is unique to this case and cannot be seen or compared to other cases This case is a case study, meaning the results cannot be generalized to the public	Japan

Continued

Kate, *et al.*, 2011 [24]	Longitudinal study	n = 1 - 22 year old Indian female with 9-day history of intermittent fever and associated abnormal behavior	18 months	DSM-IV EEG Brain MRI CSF examination Bush Francis Catatonia rating score (BFCR) Intravenous lorazepam Sodium valproate Escitalopram Bromocriptine Clozapine rTMS	Apathy nihilistic delusions repetitive movements Whole body rigidity Fever Restlessness Mute Oral cavity drooling	By the end of the patient's 20 cycles of rTMS, she had started to feel better Her BFCR scale dropped from 32 to 9 Made good eye contact Could speak fluently and coherently Minimal to no motor rigidity left Within 3 more months, there were no more signs of catatonia left and the patient returned to her normal college life	This woman had her catatonia associated with her lasting, intermittent fever, which may be more rare and harder to compare to other studies This is a case study, meaning the study results cannot be generalized to the population	India
Hagikura, Inada, 2023 [25]	Longitudinal study	n = 1 - 34 year old female who has had a history of catatonic schizophrenia and antipsychotic treatment for it. She relapsed a year later and was treated with the blonanserin transdermal patch	About 1-2 months	COVID-19 test Blood tests Brain MRI Oral benzodiazepines Blonanserin (antipsychotic transdermal patch)	Paranoid delusions of being harassed by others Decreased appetite Severe dehydration, which is why patient wouldn't take medicine orally Fatigue Motor rigidity (catatonia) Uncontrollable large periods of urination	6 - 7 days after her admission to the hospital and treatment with the blonanserin patch, the patient began to open her eyes more often and communicate better. She made head nodding movements and had better motor control. Around 2 weeks later, she was discharged with no return of catatonic symptoms	The woman had severe dehydration and consequences of uncontrollable urination as result of the blonanserin and even before its administration, which is a rare circumstance and may not compare to other studies. Blonanserin was a patch that was approved very first in Japan, so Japan has the most studies of this patch and its usefulness compared to other countries, which may serve as a confounding variable. This is a case study, meaning the results cannot be generalized to the public.	Japan

Continued

Ohi, *et al.*, 2017 [26]	Longitudinal study	n = 1 - 53 year old male with history of schizophrenia and a major stressor event in his life recently before admittance to hospital (family member death), meaning he discontinued his medication for schizophrenia	Around 1 month	DSM-IV Laboratory examinations EEG Dantrolene Intravenous (IV) infusion of midazolam Intramuscular injection of diazepam CT scan Flunitrazepam Aripiprazole	Agitation Monologue Insomnia Hyperthermia Tremor Muscle rigidity Clouded consciousness Tachycardia Hypertension Profuse sweating	After 29 days in the hospital, the patient was stable. He had received a combination of medicinal treatments, but the most important one being diazepam, which relieved the drooling, dysphagia hyperthermia, and caused muscle relaxation from its previous rigidity Patient's psychotic symptoms were relieved and he was stable.	The patient underwent a major life stressor which could have led to his relapse in schizophrenia/ catatonia The patient stopped taking his medication for 3 days prior to his admittance to the hospital, signifying that this was the most likely cause of his catatonic symptoms, which may not be very comparable to other case studies This is a case study, meaning the results cannot be generalized to the public	Japan
Unal, *et al.*, 2013	Cohort study	n = 57 30 women 27 men	8 years	DSM IV (4th edition) ECT Benzodiazepines (lorazepam) Positive and Negative Symptoms Scale Hamilton Depression Rating Scale Young Mania Rating Scale Clinical Global Impression-Improvement scale	Symptoms overall included psychosocial stressors, hallucinations Associated mood disorders Psychotic disorders Mutism Withdrawal Immobility Waxy flexibility Withdrawal Negativism	All 57 individuals were treated with ECT and benzodiazepine combined therapy and all 57 of them resolved their catatonic symptoms	Some of the participants that had catatonia had psychosocial stressors that induced their episode while others didn't	Türkiye

3. Results

3.1. Cotard's Syndrome

Research demonstrates that there are a variety of symptoms associated with Cotard's syndrome, the majority including symptoms of suicidal ideations and restricted mobility. One of the most prominent symptoms are the claims of not having certain limbs, organs, or claims of being dead. Along with these more significant, defining symptoms are more common ones, such as depressed mood, nihilistic behavior, anxiety, motor rigidity, loss of appetite, suicidal idealations, and insomnia. As seen in the [13] (Mughal *et al.*, 2013) study, the patient exhibited symptoms of suicidal feelings, claims of having a rotting corpse, claims of her limbs falling off, and psychosomatic induced immobility. In another case study, by [14] (Grover *et al.*, 2010), the patient exhibited symptoms of claimed lycanthropy (that her bones were converting to pig bones and treat she and her children overall were turning into pigs), claimed God was punishing her for skipping prayers and religious pilgrimages, and decreased sleep/insomnia due to her anxiety. Thus, a great deal of anxiety is also associated with Cotard's syndrome, similar to Illness anxiety disorder. Furthermore, in another study by [15] (Grover, *et al.*, 2014), a patient exhibited decreased appetite, nihilism, hopelessness, feelings of sin and guilt, delusions of catastrophe, poverty, and persecution. He believed he had an illness he could spread that caused cancer, which was his reasoning for his suicidal intent. Thus, we can see that there are quite a few delusions involved with all of these studies as well.

The research done on Cotard's syndrome and the articles chosen support evidence that Electroencephalography (ECT) was the major tool used to treat this disorder. ECT is usually used as a last resort to treating disorders, which signifies the severity and rarity of Cotard's syndrome. Thus, ECT was a major theme displayed throughout articles discussing the treatment of Cotard's syndrome. For example, in a case study of a woman with Fronto-Temporal Dementia (FTD) who was experiencing symptoms of Cotard's syndrome, the patient responded to 18 ECT sessions very well [3]. She claimed that she did not have her intestines, stomach, lungs, and even claimed that she was dead. However, during and after her ECT, her overall psychotic symptoms and delusions eventually stopped. Her associated sluggishness and claims of missing organs diminished completely. One side effect seen through this exhibit of ECT and many others is that there was a fluctuation in mental health. Patients often experience depressive symptoms fluctuating throughout the ECT treatment, but they often disappear by the end of the treatment. Another widely used therapy for Cotard's syndrome is antipsychotic (olanzapine), antidepressant, and ECT combination therapy. In the Mughal, Menezes study, a patient who experiencing nihilism, suicidal idealizations, claims of feeling like a rotting corpse, and psychosomatic induced motor rigidity, had completely resolved her symptoms with antipsychotic, antidepressant, and ECT combination therapy [13]. The patient felt much happier as well as attended to her personal hygiene, and her motor disability was completely re-

paired. Similar results were seen in the Weiss study which used Olanzapine (an antipsychotic drug) which successfully alleviated all symptoms of Cotard's syndrome [16].

Overall, the most commonly used treatments for Cotard's syndrome include ECT (electro-convulsive therapy), Lorazepam (an anti-anxiety medication), and Olanzapine (an antipsychotic medication), or a combination of an antidepressant, anti-anxiety medication, and ECT.

The only side effects mentioned in the articles are mood and mental health fluctuation, which was exhibited in the Kobayashi case study [2]. While Cotard's syndrome commonly has depression as a side effect, the use of ECT sometimes worsens it or causes bipolar-like symptoms, in which changes in mood are frequent and unexpected, as seen in the case study mentioned.

3.2. Alice in Wonderland Syndrome (AIWS)

The articles selected demonstrate that the symptoms associated with Alice in Wonderland Syndrome are mainly pertaining to the visual field. These symptoms are also associated with other disorders. Alice in Wonderland Syndrome itself is often presented as a symptom of some other neurological disorder. For example, in the Tunç, Başbuğ study, the patient had a history of migraines and severe headaches as a child, along with a maternal family history of them [18]. Her AIWS symptoms were suspected to have arisen because of these migraines, as a symptom. Furthermore, in the Uca, Kozak study, the patient had a history of cluster headaches, another neurological condition inducing AIWS [19]. Finally, in the Mastria study, a patient who had glioblastoma (a type of brain cancer) experienced symptoms of AIWS [21]. However, his symptoms disappeared after his tumor was removed and went into remission, suggesting that the AIWS symptoms were only present due to the severe neurological condition. Because of the severity of these neurological disorders and their wide range of symptoms, it is commonly seen that distortions in the visual field may arise, such as micropsia (seeing things smaller than they actually are), macropsia (seeing things larger than they actually are), and perception of inaccurate colors or 'auras', as mentioned in the Tunç, Başbuğ study [18].

The actual symptoms of Alice in Wonderland Syndrome, as mentioned before, mainly include micropsia, macropsia, perception of different colors, distorted sense of speed or time, distorted perception of size, migraines, headaches, depressed mood, and distorted body image. As seen in the Yokoyama study, severe and consistent periods of depression, altered body image, and altered perceptions of speed and time were frequent in the patient [17]. Furthermore, the patient also portrayed interesting symptoms of a lack of empathy and value. He was able to know the value of money and people but not feel it. Other than this, as the Tunç, Başbuğ study suggests, the patient experienced frequent misconceptions of size and auras [18]. She claimed that she saw her father's head as large and having a blue aura. Finally, the Uca, Kozak study also suggests that the pa-

tient experienced distortions of speed, color, and size minutes before his migraine attacks [19].

The research done on the treatments of Alice in Wonderland Syndrome supports the evidence that Valproate (an anti-epileptic drug) is the most effective. Most of the articles chosen had a variety of different treatments, yet Valproate was the only one that reappeared multiple times. First, the Uca, Kozak study treated their patient with Valproate for 3 months, which yielded improved clinical conditions through a complete loss of headaches (thus removing all associated AIWS symptoms, in this case, visual hallucinations) [19]. Therefore, we can see that Valproate is mainly used as an attempt to relieve the cause of AIWS, the neurological disorders (migraines and headaches). Valproate was also used to treat the patient in the Hamed study, which was prescribed to the patient for a long duration of time and will likely continue for the rest of their life to reduce the severity of the headaches [20]. Lastly, Valproate was also used to treat the glioblastoma patient in the Mastria study [21]. After prescription of Valproate as well as the neurosurgery and drug chemotherapy for the cancer, the patient's symptoms completely vanished and had no other recurrences of AIWS symptoms.

Overall, it is clear that Valproate is the most commonly used treatment for AIWS, but only applies to cases in which AIWS is associated with some other neurological condition, such as headaches, migraines, or tumors.

There seem to be no significant or notable side effects to the use of Valproate mentioned in the articles chosen. The overall impact seems to be positive and effective within a few months of treatment.

3.3. Catatonic Schizophrenia/Catatonia

The research exemplifies that Catatonic Schizophrenia/Catatonia's symptoms are widely associated with motor rigidity and psychosomatic-induced motor retardation. These include widely negative symptoms of schizophrenia, such as waxy flexibility, mutism and the flat effect. Wavy flexibility means that patients with Catatonia often are able to stay frozen or completely still in odd positions for as long as days at a time. The flat effect signifies a lack of emotion and expression variability. As seen in the Chen study, the patient experienced catalepsy, mutism, agitation, grimacing, hyperthermia, and motor rigidity as symptoms of their Catatonia [22]. The patient had been diagnosed with Catatonia ten years prior, but his symptoms showed no improvement from the use of benzodiazepines and antipsychotics. Thus, his motor rigidity was able to last for long periods on end with no effective treatment up until then. Furthermore, according to the Nomura study, the patient experienced strong motor rigidity in the upper and lower limbs, as well as verbal rigidity [23]. Thus, the physical and verbal rigidity and lack of expression are significant in Catatonia patients. This physical rigidity can also have associated effects. For example, in the Kate study, the patient experienced oral cavity drooling, nihilistic delusions, depression, restless-

ness, and fever [24]. Thus, depression and oral cavity drooling are common symptoms or associated symptoms of Catatonia. Furthermore, uncontrolled urination, inability to maintain personal hygiene, and anxiety are also common effects. In the Hagikura, Inada study, the patient experienced uncontrollable large periods of urination as well as dehydration and weight loss because she would refuse to eat or drink anything due to her severe state of immobility [25]. This also meant that she refused to take medicines orally, which led to alternative methods being proposed for her treatment. In the Ohi study, the patient experienced hyperthermia, immobility, hypertension, and profuse sweating [26]. We can see that hyperthermia and associated body impairments are frequent in Catatonia patients. Finally, in the Unal cohort study, the majority of the patients experienced symptoms of negativism, withdrawal, waxy flexibility, and associated mood disorders or fluctuations [27].

It is also important to note that quite a few patients had been diagnosed with Catatonia for years, or even decades, prior and were in remission. However, because of psychosocial stressors (*i.e.* in the Ohi study, the patient stopped taking his medication for Catatonia because of a major life stressor) [26].

The articles selected overall support the effectiveness of ECT (electro-convulsive therapy) and benzodiazepine therapy in combination, as well as rTMS (rapid transcranial magnetic stimulation). benzodiazepines used to treat Catatonia had already been an established, common first-base treatment for newly diagnosed patients. However, it is not always effective and sometimes loses its effectiveness over time, which is why ECT and rTMS are now widely discussed treatments as well. According to the Kate study, which used rTMS as their method of treatment, all of the patient's symptoms of verbal/motor rigidity had diminished, and her Bush Francis Catatonia rating score (BFCR) score had dropped from 32 to 9 by the end of treatment [24]. The patient was able to speak fluently again by the end as well. Furthermore, as the Ohi study discusses, the patient was treated with a variety of treatments but mostly with diazepam (a benzodiazepine drug) which resulted in his remission [26]. The diazepam treatment resulted in the patient's ability to move again and stop drooling (which was a side effect of his prior severe motor rigidity). The patient's motor flexibility completely returned by the end of his hospital stay. Not only this, but the Unal study provides concrete evidence of the effectiveness of benzodiazepines in combination with ECT [26]. Since the study is a cohort study and involves multiple (57) people with Catatonia, it provides results that are generalizable to the population of Catatonia patients. The treatment of benzodiazepines and ECT in combination yielded a 100% successful recovery in all Catatonia patients over a span of eight years. Thus, it is evident that benzodiazepines and ECT are largely successful in treating Catatonia.

It is also important to mention alternative treatments used to treat special cases of Catatonia. For example, in the Hagikura, Inada study, the patient's Catatonia was so severe that they refused to take drug treatment orally, as she re-

fused to open their mouth [25]. Thus, in Japan, the blonanserin patch (an antipsychotic transdermal patch that can be applied on the skin) was used. The blonanserin patch was first globally approved for use in Japan in 2019. The patch proved to be effective, as the patient resolved her Catatonic symptoms within two weeks of administration. The patient was able to open her mouth, communicate verbally, and develop better motor control.

There do not seem to be any significant side effects of benzodiazepines and ECT in combination that were mentioned. However, the blonanserin patch yielded larger, uncontrollable amounts of urination and profuse sweating. Overall, the blonanserin patch proved effective in subsiding the symptoms of Catatonia, however, it also led to larger amounts of liquid secretion from the body (urination, sweating).

4. Discussion and Conclusions

4.1. Overall Results

It is clear that ECT is a very popular mode of treatment for both Cotard's Syndrome and Catatonic Schizophrenia/Catatonia. This is likely because of the fact that they both include psychotic symptoms. Furthermore, the symptoms themselves presented seem to share similarities across all 3 disorders. For example, all 3 disorders result in some sort of depression, depressed mood, anxiety, and mood swings. This is also likely due to the severity and rarity of the disorders chosen. Furthermore, both Alice in Wonderland Syndrome (AIWS) and Cotard's syndrome involve delusions and hallucinations, as they share similar symptoms of distorted perceptions of reality. In fact, Type 1 of AIWS follows a similar pathway as Cotard's Syndrome does. Type 1 of AIWS is defined as people feeling as though their own body parts are changing in size, while Cotard's syndrome is defined as feeling as though their body parts are missing or dead.

Furthermore, insomnia also seems to be a side effect of all 3 disorders chosen. Once again, because of the highly debilitating nature of the disorders chosen, they are known to cause insomnia. This is also because of the associated symptoms of all 3 disorders. For example, patients with Cotard's syndrome are often stuck in odd, difficult positions which may inhibit their ability to relax and sleep. Furthermore, patients with AIWS often experience neurological pain such as headaches, migraines, or tumors which may contribute to their lack of sleep. Lastly, Cotard's syndrome typically results in substantial anxiety about being dead or dying, which may also contribute to the development of insomnia.

It is also significant to note that the majority of the studies conducted on all 3 disorders were done in Japan (5 out of 16 articles), and that Latin America and Africa are not represented in any of the articles searched for. Thus, Latinos and Africans are a widely underrepresented demographic in studies of Cotard's syndrome, AIWS, and Catatonia.

From this data, it can be concluded that ECT seems to be the most common

mode of treatment, currently, for Catatonia and Cotard's Syndrome. However, it is more common for benzodiazepines, antipsychotics, and or anticonvulsants to be used to treat Alice in Wonderland Syndrome. The most common one seen is Valproate, which is originally used to prevent seizures or the manic mood swings of bipolar disorder.

4.2. Cotard's Syndrome: Gaps in Existing Research

There seem to be quite a few geographical areas that are underrepresented in the studies conducted on Cotard's Syndrome. As mentioned before, there are no studies included or found that have been conducted on people of African or Latino ethnicity or descent. This demographic discrepancy may be attributed to the lack of resources funded to do research in these regions or the lack of resources available to get the treatments required for people of African and Latino backgrounds. There seems to be a high density of studies from Asia, including Japan and India. There are also studies from the United States and the United Kingdom. Furthermore, in regards to gender, there seems to be more women with Cotard's syndrome that are studied than men (4 women, 2 men included in the article studies). Thus, men and people of Latino and African backgrounds are underrepresented demographics in the studies of potential treatments for Cotard's syndrome.

4.3. Alice in Wonderland Syndrome (AIWS): Gaps in Existing Research

The same geographical areas are underrepresented in studies of Alice in Wonderland Syndrome. The Latino and African communities are, once again, underrepresented in these studies. There also seem to be more men represented in studies of AIWS than are women (4 men, 1 woman identified in the studies). Thus, women and people of Latino and African backgrounds are underrepresented demographics in the studies of the current and upcoming treatments for AIWS. The articles chosen originate in Japan, Turkey, Egypt, and Italy.

Furthermore, it is important to note that the majority of patients of AIWS had an associated neurological disorder that caused or influenced the development of their AIWS symptoms. For example, in the Tunç, Başbuğ study, the patient had a history of migraines [18]. In the Uca, Kozak study, the patient had a history of cluster headaches [19]. In the Matria study, the patient had a brain tumor. All of these neurological conditions are believed to have caused the onset of AIWS symptoms in the patients. Thus, their AIWS symptoms often subsided as their associated neurological conditions diminished in severity.

It is also important to note that many of the patients of AIWS have a personal history of neurological disorders, but not a family history of them.

4.4. Catatonic Schizophrenia/Catatonia: Gaps in Existing Research

The same geographical areas are underrepresented in studies of treatments for

Catatonia. The Latino community and African community are, once again, an underrepresented and understudied demographic. The countries that are represented in the studies conducted include the United States, India, Japan, and Turkey. Interestingly enough, Japan was represented in half of the articles (3 out of 6) chosen for Catatonia. Furthermore, there are roughly an equal number of men and women represented for studies of Catatonia, so there is little or no discrepancy in gender in these studies.

5. Limitations

The major limitations of this scientific literature review are due to the rarity of the conditions chosen, signifying that there were not many studies done on these conditions, especially not on their treatment. Most studies done are preliminary and only examine the symptoms and causes of these conditions, but are too early on and limited with studies to conduct significant studies of their treatments. Furthermore, the studies' applicability and generalization are limited due to the fact that 15 out of 16 of the articles were case studies. Because they are case studies, the advantages are that they provide much more detail and insight into the effects of the treatments and the timeline follower. However, the disadvantage is that most case studies are only relevant to the patient, meaning they cannot be applicable to others who share the same disorder. Case studies are often done because the circumstances are unique, such as the Kobayashi study, in which the patient had Fronto-Temporal Dementia (FTD) associated with her Cotard's syndrome [3]. Thus, these studies share limited similar symptoms and treatment options compared to other studies. The only study selected which could be generalizable was the Unal study, which involved 57 participants and was a cohort study [27].

Furthermore, there were limitations regarding the accessibility of resources in this study. This review was conducted using only free, online texts and PDFs as resources. So, there could have been more conclusive evidence offered if paid materials were used. This review was also conducted within the confinements of an English language requirement, so studies in other languages or translations were excluded. These studies could have also presented valuable information for inclusion, but were not for the sake of ease of comprehension of material.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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