Cognitive-behavioural therapy of obsessive-compulsive disorder

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Cognitive-Behavioural Therapy of Obsessive-Compulsive Disorder

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ABBREVIATIONS USED IN THE TEXT:

Behaviour Therapy (BT)

Bibliotherapy administered CBT (bCBT)

Cognitive-Behavioural Therapy (CBT)

Cognitive Therapy (CT)

Computerized CBT (cCBT)

Danger Ideation Reduction Therapy (DIRT)

Deep Brain Stimulation (DBS)

Diagnostic and Statistical Manual of Mental Disorders (DSM-5)

Exposure and Response Prevention (ERP)

Generalized Anxiety Disorder (GAD)

International Classification of Disease (ICD-10)

Internet-administered CBT (iCBT)

Major Depressive Disorder (MDD)

Monoamine Oxidase Inhibitors (MAO)

Obsessive-Compulsive Disorder (OCD)

Obsessive-Compulsive Personality Disorder (OCPD)

Selective Serotonin Reuptake Inhibitor (SSRI)

Serotonin; 5-hydroxytryptamine (5HT)

Serotonin Reuptake Inhibitor (SRI)

Subjective Units of Distress Scale (SUDS)

Telephone administered CBT (tCBT)

Tricyclic Antidepressants (TCA)

Videoconferencing administered CBT (vCBT)

Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)

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1. SUMMARY

Title: Cognitive-Behavioural Therapy of Obsessive-Compulsive Disorder

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Obsessive-Compulsive disorder is a severe and debilitating psychiatric disorder affecting more and more people worldwide. As the fourth most common psychiatric disorder, its history can be traced back to the 16th century. Although previously classified as an anxiety disorder in DSM-IV, it has recently been given its own chapter with related disorders in DSM-5. In ICD-10, OCD is grouped with neurotic, stress-related and somatoform disorders, and given the code F42. ICD-10 subdivides OCD into three types: predominantly obsessive type, predominantly compulsive type, and the most commonly found mixed type. Obsessions can be defined as repetitive and persistent thoughts or feelings that are viewed by the patient as intrusive and inappropriate and cause marked anxiety or distress. Typical obsessions include: fears of being contaminated by germs or poisons, fears of causing harm to oneself or others, and fears of committing some unacceptable action. Compulsions, on the other hand, are repetitive acts or behaviours that the patient deems necessary to perform as a response to an obsession, and which serve to reduce anxiety. Common compulsions include: excessive washing and cleaning, checking, seeking reassurance, hoarding objects, and insisting that things be put in a specific order or pattern. Based on the severity of symptoms OCD can be divided into mild, moderate and sever forms. Many theories exist on the etiology of OCD, but no theory is regarded as the sole etiologic factor. Comorbidity with other psychiatric disorders is common, with a lifetime history of major depression present in two thirds of OCD patients. An array of different psychiatric and neurologic disorders must be taken into account in the differential diagnosis of OCD such as: specific phobias, major depressive disorder, trichotillomania, hoarding disorder, tic disorders, and obsessive-compulsive personality disorder. The primary goal of treatment in the majority of OCD cases is to have the individual control the disorder rather than the obsessional disorder control the individual. Safe and effective first-line treatment for OCD includes cognitive-behavioural therapy (CBT) and pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs). Severe and drug-resistant cases can be managed with electroconvulsive therapy and rarely, surgery. The course of the disease is chronic, and the quality of life largely depends on the severity of symptoms and the response to therapy.

Keywords: obsessive-compulsive disorder, differential diagnosis, pharmacotherapy, cognitive-behavioural therapy

2. SAŽETAK

Naslov: Kognitivno-behavioralna terapija opsesivno-kompulzivnog poremećaja

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Opsesivno-kompulzivni poremećaj (OKP) je teški i debilitativni psihijatrijski poremećaj koji utječe na sve više i više ljudi širom svijeta. Kao četvrti najčešći psihijatrijski poremećaj, njegova povijest se može pratiti do 16. stoljeća. Iako je prethodno klasificiran kao anksiozni poremećaj u DSM-IV, nedavno je dobio vlastito poglavlje s povezanim poremećajima u DSM-5. Kod ICD-10, OKP je grupiran s neurotskim, stresnim i somatoformnim poremećajima, te dodijeljen kod F42. ICD-10 dijeli OKP u tri tipa: pretežno opsesivno tip, pretežno kompulsivan tip i najčešće pronađen mješoviti tip. Opsesije se mogu definirati kao ponavljajuće i perzistentne misli ili osjećaje koje pacijent doživljava kao intruzivne i neprimjerene te koji uzrokuju ozbiljnu tjeskobu ili nelagodu. Tipične opsesije uključuju: strah od onečišćenja ili kontaminacije, strahovanja od nanoseći zla sebe ili drugima, i strah od počinjenja nekog neprihvatljivog djelovanja. S druge strane, Kompulzije ili prisile su ponavljajuća djela ili ponašanja koji pacijent smatra potrebnim za obavljanje kao odgovor na opsesiju, a koji služe za smanjenje anksioznosti. Uobičajene prisile uključuju: pretjerano pranje i čišćenje, provjeravanje, traženje sigurnosti, sakupljanje predmeta i inzistiranje na tome da se stvari stave u određeni red. Mnoge teorije postoje na etiologiji OKP, ali niti jedna teorija ne smatra se superiorna nad ostalim. Komorbiditet s drugim psihijatrijskim poremećajima je uobičajen, s dugotrajnom poviješću velike depresije prisutne u dvije trećine pacijenata s OKP. Različiti psihijatrijski i neurološki poremećaji moraju se uzeti u obzir u diferencijalnoj dijagnozi OKP-a, kao što su: specifične fobije, depresija, trichotilomania, patološko skupljanje, tic poremećaji i opsesivno-kompulzivni poremećaj ličnosti. Primarni cilj liječenja je da pojedinac kontrolira poremećaj, a ne da poremećaj kontrolira pojedinca. Sigurno i učinkovito prvoklasno liječenje OKP-a uključuje kognitivno-bihevioralnu terapiju (KBT) i farmakoterapiju sa selektivnim inhibitorima ponovne pohrane serotonina (SIPPS). Teški slučajevi otporni na lijekove mogu se liječiti elektrokonvulzivnom terapijom, a rijetko, kirurški. Tijek bolesti je kroničan, a kvaliteta života uvelike ovisi o težini simptoma i odgovoru na terapiju.

Ključne riječi: opsesivno-kompulzivni poremećaj, diferencijalna dijagnoza, farmakoterapija, kognitivno-bihevioralna terapija

3. INTRODUCTION

Obsessive-compulsive disorder has a long history stretching back to the sixteenth century. Shakespeare himself incorporated the disorder in his play Macbeth. In the play, the character of Lady Macbeth washes her hands repeatedly in an effort to reduce her distress after she prods her husband to murder Scotland's king. Even earlier, people with obsessions and compulsions were believed to be possessed by the devil. Exorcism was the treatment of choice, during which the person was subjected to torture in order to drive out the intruding entity. By the 1700s, the cause of obsessions and compulsions moved from a religious to a medical view. Doctors began performing procedures such as bloodletting in an attempt to try and cure their patients from obsessive thoughts. In the 1800s, it became much more common to institutionalize the mentally ill, and this unhappy development also affected many OCD sufferers. In 1838, obsessions and compulsions were first described in psychiatric literature by French physician J.E.D. Esquirol, and were regarded as manifestations of melancholy or depression. By the beginning of the twentieth century, the view of OCD had shifted toward a psychologic explanation. This was partly due to the French psychiatrist Pierre Janet and the Austrian psychiatrist Sigmund Freud. Sigmund Freud attributed obsessive–compulsive behaviour to unconscious conflicts that manifest as symptoms. He conceptualized the disorder as a conflict between the *ego* and *superego*, or aggressive and sexual impulses emerging from the *id* manifesting symptoms of obsessions as a punishment sent by the *superego* (Kempke & Luyten, 2007). In the last decades of the twentieth century, with the development of modern neuroimaging and neurochemical methods, the biology of this disorder began to be explored. Today a variety of models and hypotheses have been proposed in an attempt to explain the development of OCD including the serotonin hypothesis, neuroanatomical models, and behavioural theories. Several different lines of research also point towards genetic factors.

OCD is a condition in which the patient has either obsessions, compulsions, or both. These can be so frequent or intense that they interfere with the patients social or role functioning. The first symptoms usually appear in early adulthood and have an impact on the patient’s quality of life. OCD is the fourth most common psychiatric disorder in the population and thus represents a social and economic burden in today's society. It is usually a chronic disorder, but with the help of today's pharmacological and psychotherapy approaches, symptoms can be controlled and the disorder managed.

4. EPIDEMIOLOGY

OCD was once thought to be a rare disorder in the general population. This perception was based on an epidemiologic study by Rudin, who estimated OCD prevalence to be 5 in 10,000 in the general population (Stein et al., 2010). Several studies completed in the late 1950s and early 1960s examined the frequency of psychiatric diagnoses of OCD in inpatient and outpatient settings and further reinforced this false belief. The two largest epidemiolgical studies by Karno et al. in 1988 and Weissman et al. in 1994 utilized trained lay interviewers to administer a structured diagnostic interview. They found that the one year OCD prevalence rates ranged from 0.8 % to 2.3 % (URL-1). However, the most recent epidemiological data from DSM-5 indicates that the 12-month prevalence of OCD in the United States is 1.2 %, with a similar prevalence internationally: 1.1 - 1.8 % (DSM-5, 2013). Females are affected at a slightly higher rate than males in adulthood, although males are more commonly affected in childhood. The first symptoms of OCD usually appear before the age of 25 in more than two thirds of cases, while for less than 15 % of patients they appear after the age of 35 (Rasmussen and Eisen, 1992). The course of the disorder when untreated is generally chronic, with waxing and waning of symptoms. Some individuals have an episodic course, and a minority have a deteriorating course. Stress appears to exacerbate the condition. Many adults with the disorder have a lifetime diagnosis of an anxiety disorder (76 %; e.g., panic disorder, social anxiety disorder, generalized anxiety disorder, specific phobia) or a depressive or bipolar disorder (63 % for any depressive or bipolar disorder, with the most common being major depressive disorder - 41 %)(DSM-5, 2013). Up to 30 % of individuals with OCD also have a lifetime tic disorder. A comorbid tic disorder is most common in males with onset of OCD in childhood.

5. ETIOLOGY

The etiology of OCD is still a mystery for doctors today. There are many theories on what might be the cause OCD, but no theory is regarded as the sole etiologic factor.

5.1. Psychological Etiologies

5.1.1. Psychodynamic Theory

This theory was created by Freud in an attempt to explain the symptoms of OCD. He focused his attention on the mother-infant interaction and considered issues of aggression and autonomy to be paramount around the time of toilet training, when the child strives to hold on to valuable feces and the mother requests that he give them up to please her. Freud developed concepts of anality and anal sadism and proposed that hostile impulses against the parents were controlled by obsessive-compulsive behaviour (Jenike et al., 1998).

5.1.2. Behavioural Theory

The behavioural conceptualization of OCD emphasizes the role of conditioning in the development and maintenance of the disorder (Salkovskis & Kirk, 1989). According to this theory, obsessions are produced when a previously neutral object becomes associated with a stimulus that produces fear. Compulsions follow as the individual attempts to reduce the anxiety produced by the learned fearful stimulus. Avoidance of the object and performance of compulsions reinforces the fear and perpetuates the vicious cycle of OCD.

5.1.3. Cognitive Theory

A primary feature of this model is that particular types of intrusive thoughts, upon appraisal, will interact with beliefs of responsibility in vulnerable individuals and lead to behaviours designed to neutralize the threat posed by the obsessional thought. Central to this theory is the

notion of responsibility. Salkovskis and Kirk place particular emphasis on resonsibility, pointing out that schemas of danger, in the absence of percieved responsibility, will lead to other forms of anxiety disorders other than OCD (Salkovskis & Kirk, 1997).

5.2. Biological Etiologies

In 1964, several studies were conducted to observe the relationship between neurologic illness and obsessional disorders. Grimshaw studied 103 obsessional patients and reported that 19.4 % had a history of neurologic illness compared with only 7.6 % of a control group of 105 normal subjects (a significant differnce; p=0.05) (Grimshaw, 1964).

5.2.1. Immunologic Hypothesis

In Grimshaw's study, six OCD patients had serious central nervous system infections, eight had a history of convulsive disorder and six patients had a history of chorea consistent with Syndehams chorea. In a more recent study by Rapoport, approximately 20 % of rheumatic fever patients develop Syndenham's chorea, probably as a result of an autoimmune response to the basal ganglia, leading to potential damage in that area (Rapoport, 1989). Obsessional symptoms were significantly higher among those patients with Sydenham's chorea. In children, such symptoms have been called paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). It is believed that this results when antibodies directed against invading streptococcus bacteria cross-react with basal ganglia structures, resulting in onset or exacerbation of OCD or tic disorder.

5.2.2. Association with Hypothalamic Lesions

A study conducted by Pitman, using rats, showed that bilateral hippocampal lesions produce repetitive behaviours, invariability, excesiveness, retarded extinction, and improved shuttle-

box avoidance (Pitman, 1982). He believed that the symptoms in the animals were not coincidental and that there is a similarity between the symptoms and behaviour of OCD individuals.

5.2.3. Metabolic Changes in Corticostriatal Circuitry

Neuroimaging studies of OCD have shed considerable light on the neuroanatomical structures involved in the expression of OCD. Functional imaging studies have shown increased activity in the corticostriatal pathway involving anterior/lateral orbitofrontal cortex and the caudate nucleus, which is accentuated during symptom provocation and attenuated following effective treatment. (Jenike et al., 1998).

5.2.4. Amygdalocentric Models

The amygdala is one of two almond-shaped groups of nuclei located deep and medially within the temporal lobes of the brain. It is a structure that has been implicated in emotional fear conditioning. Through the evidence collected from various animal studies, it has been proposed that the amygdala is a key neuroanatomic substrate of the anxiety that perpetuates compulsions in OCD (Whalen and Kapp, 1991).

5.2.5. The Serotonergic Hypothesis

Serotonin is a monoamine neurotransmitter that is primarily thought to be responsible for feelings of well-being and happiness. The serotonin hypothesis suggests that 5HT dysregulation may be etiologically linked to OCD. Although there is not yet any compelling data to support this hypothesis, serotonergic medication have been proven to be effective as treatments for OCD. One study found that the therapeutic effects of 5HT are correlated with changes in peripheral parameters of function, which have been found to be altered in OCD, suggesting the possibility of reduced 5HT reuptake capacity. This could reflect a

compensatory mechanism presumably due to decreased availability of extracellular 5HT, as evidenced by data derived from direct assessment of central 5HT neurotransmission (Aouizerate et al., 2005).

5.2.6. The Glutamatergic Hypothesis

Recent evidence suggests that the excitatory neurotransmitter glutamate is dysregulated in OCD. The most direct evidence for excessive glutamatergic activity in OCD derives from a recent study examining CSF from patients with OCD. Chakrabarty et al.examined the CSF of 21 drug-naive OCD patients and 18 control subjects, and found CSF glutamate levels to be significantly elevated in those subjects with OCD. (Chakrabarty et al., 2005).

5.2.7. Genetics

The evidence for possible genetic predisposition in OCD derives from two sources: twin studies and investigations of the first degree relatives of OCD sufferers. To date, the largest and most statistically robust twin study found a monozygotic twin concordance rate of 0.52 and a dizygotic concordance rate of 0.21, with overall heritability for OCD estimated to be 48 % (Brown et al., 2014). Furthermore, first degree relatives of patients with OCD are more likely to suffer from OCD than are the relatives of psychiatric controls. Recurrence risk among first-degree relatives for lifetime OCD estimates to be as low as 6 % to as high as 55 %, with the majority of estimates falling between about 10 and 20 % (Brown et al., 2014). These estimates are significantly higher than the lifetime prevalence for OCD in the general population, which is estimated to be 0.7-3 % (Brown et al., 2014). Overall, the evidence suggests that genetic factors play a role in the disorder.

6. CLINICAL PICTURE

OCD is a condition in which the patient has either obsessions, compulsions, or both. These can be so frequent or intense that they interfere with the patients social or role functioning. Obsessions are recurrent and persistent thoughts, urges, or images that are experienced as intrusive and unwanted, whereas compulsions are repetitive behaviours or mental acts that an individual feels driven to perform in response to an obsession, or according to rules that must be applied rigidly (DSM-5, 2013). As well as being intrusive and unwanted, obsessions cause marked distress and anxiety in most individuals. Typical obsessions include: fears of being contaminated by germs or poisons, fears of causing harm to oneself or others, and fears of committing some unacceptable action. While on the other hand, compulsions are typically performed in response to an obsession with the aim of reducing the distress or to prevent a feared event (Leahy et al., 2012). Usual compulsions include: excessive washing and cleaning, checking, seeking reassurance, hoarding objects, and insisting that things be put in a specific order or pattern. The majority of pateints have both obsessions and compulsions. It is common for individuals with the disorder to avoid people, places, and things that trigger obsessions and compulsions. Comorbidity with other psychiatric disorders is common, with a lifetime history of major depression present in two thirds of OCD patients. Suicidal thoughts occur at some point in as many as about half of individuals with OCD. Suicide attempts are also reported in up to one-quarter of individuals with OCD; the presence of comorbid major depressive disorder increases the risk (DSM-5, 2013). This disorder also coexists with a number of other Axis I disorders including panic disorder, social phobia, eating disorders, and Tourette's disorder (Rasmussen & Eisen, 1992). A clinician administered rating scale exists called the Y-BOCS. It has become the most widely used rating scale for OCD and is designed to rate symptom severity, not to establish a diagnosis. The Y-BOCS provides five rating dimensions for obsessions and compulsions:

time spent or occupied, interference with functioning or relationships, degree of distress, resistance, and control (i.e., success in resistance). The 10 Y-BOCS items are each scored on a four-point scale from 0 = no symptoms to 4 = extreme symptoms. The sum of the first five items is a severity index for obsessions, and the sum of the last five an index for compulsions. A translation of total score into an approximate index of overall severity is: 0-7 = subclinical, 8-15 = mild, 16-23 = moderate, 24-31 = severe, 32-40 = extreme (URL-2). The scale is useful as an initial assessment of the severity of OCD, and also as a tool to further follow the patient and their response to therapy.

7. DIAGNOSIS

The diagnosis of OCD is made when the patient fulfills the diagnostic criteria in anyone of the psychiatric diagnostic manuals that are currently being used.

7.1. ICD-10

Grouped with neurotic, stress-related and somatoform disorders, OCD is given the code F42. OCD with predominantly obsessional thoughts or ruminations is given the code F42.0, while the form with predominantly compulsive actions (obsessional rituals) is F42.1. The most common form is the mixed form, and this can be found under code F42.2.

7.2. DSM-5

Compared to the previous DMS-IV version, in DMS-5 OCD has been given its own chapter with related disorders. These include: body dysmorphic disorder, hoarding disorder, trichotillomania, excoriation disorder, substance/medication-induced obsessive-compulsive and related disorder, obsessive-compulsive and related disorder due to another medical condition, and other specified obsessive-compulsive and related disorder and unspecified obsessive-compulsive and related disorder (e.g., body-focused repetitive behavior disorder, obsessional jealousy). The diagnostic criteria of OCD according to DSM-5 are the following:

A. Presence of obsessions, compulsions, or both:

Obsessions are defined by (1) and (2):

1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.

2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).

Compulsions are defined by (1) and (2):

1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.

2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive. Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in

hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

Specify if:

With good or fair insight: The individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.

With poor insight: The individual thinks obsessive-compulsive disorder beliefs are probably true.

With absent insight/delusional beliefs: The individual is completely convinced that obsessive-compulsive disorder beliefs are true.

Specify if:

Tic-related: The individual has a current or past history of a tic disorder.

8. DIFFERENTIAL DIAGNOSIS

Differential diagnosis of obsessive compulsive disorder includes: generalized anxiety disorder, specific phobias, major depressive disorder, trichotillomania, hoarding disorder, tic disorders, and obsessive-compulsive personality disorder.

8.1. Generalized Anxiety Disorder

Adults with GAD often worry about every day, routine life circumstances, such as possible job responsibilities, health, and finances, whereas children with the disorder tend to worry excessively about their competence or the quality of their performance. Although recurrent thoughts and repetitive behaviours can also occur in GAD, the recurrent thoughts are usually about real-life concerns and future events, whereas in OCD they can be odd and irrational in nature and take the form of intrusive and unwanted thoughts, urges, or images. As with OCD, individuals with GAD have excessive anxiety that often interferes with daily functioning. However, to make the diagnosis of GAD, the anxiety and worry need to be accompanied by at least three of the following additional symptoms: restlessness, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and disturbed sleep.

8.2. Specific Phobias

In specific phobias, there is marked fear or anxiety about a specific object or situation. Most common phobias include: fear of specific animals, natural environment, or blood-injection injury. As in OCD, the fear or anxiety in specific phobias is out of proportion to the actual danger that the object or situation poses, and the individual actively avoids the situation in order to avoid the anxiety associated with it. If an individual's primary fear or anxiety is of an object or situation as a result of obsessions (e.g., fear of blood due to obsessive thoughts about

contamination from blood-borne pathogens [i.e., HIV]; fear of driving due to obsessive images of harming others), and if other diagnostic criteria for obsessive-compulsive disorder are met, then obsessive-compulsive disorder should be diagnosed (DSM-V, 2013).

8.3. Major Depressive Disorder

MDD is the most frequent comorbid condition in OCD. Most patients report the onset of depression after the appearance of the OCD (Kolada et al., 1994). The essential feature of a major depressive episode is a period of at least 2 weeks during which there is either depressed mood or the loss of interest or pleasure in nearly all activities. The individual must also experience at least four additional symptoms drawn from a list that includes changes in appetite or weight, sleep, decreased energy etc…

8.4. Trichotillomania

According to DSM 5, trichotillomania is characterized by recurrent pulling out of one's hair resulting in hair loss, and repeated attempts to decrease or stop hair pulling. The condition is found predominantly in females and it usually develops at an early age; from adolescence to early twenties. The compulsive behaviour in trichotillomania is limited to hair pulling, in the absence of obsessions.

8.5. Hoarding Disorder

Hoarding disorder is characterized by persistent difficulty discarding or parting with possessions. The main reasons given for these difficulties are the perceived utility or aesthetic value of the items or strong sentimental attachment to the possessions. In OCD, if there is acquisition of items, this is usually due to a specific obsession. Unlike in hoarding disorder,

these items are usually bizarre in nature and include: trash, feces, urine, nails, hair, used diapers, or rotten food.

8.6. Tic Disorders

A tic is a sudden, rapid, recurrent, nonrhythmic motor movement or vocalization. Tic disorders include: Tourette's disorder, persistent (chronic) motor or vocal tic disorder, and provisional tic disorder. Differentiating obsessive-compulsive behaviors from tics may be difficult. Usually in OCD there is a cognitive based drive to the behaviour and the need to perform the action a certain number of times in a particular way.

8.7. Obsessive-Compulsive Personality Disorder

OCPD (DSM-IV) or Anankastic Personality Disorder (ICD-10, F60.5) can be divided into three subtypes: obsessional, compulsive, or obsessive-compulsive. This personality disorder is characterized by a general pattern of concern with orderliness, perfectionism, excessive attention to details, mental and interpersonal control, and a need for control over one's environment. These individuals are excessively careful and prone to repetition, paying extraordinary attention to detail and repeatedly checking for possible mistakes. OCPD is one of the most common personality disorders in the general population, being found twice as often in males. OCD is usually easily distinguished from obsessive-compulsive personality disorder by the presence of true obsessions and compulsions.

9. TREATMENT

The primary goal of treatment in the majority of OCD cases is to have the individual control the disorder rather than the obsessional disorder control the individual. Achievement of this goal allows patients to reach their full potential and improve their quality of life and social or role functioning. The Y-BOCS scale is useful as an initial assessment of the severity of OCD, and also as a tool to further follow the patient and their response to therapy. If a rating scale is not used, it is helpful to document the patient's estimate of the number of hours per day spent obsessing and performing compulsive behaviours and the degree of effort applied to trying to escape the obsessions and to resisting the behaviours. In choosing a treatment approach, the clinician should consider the patient's motivation and ability to comply with pharmacotherapy and psychotherapy. Safe and effective first-line treatment for mild or moderate OCD includes cognitive-behavioural therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs). Many patients with OCD also benefit from educational materials and access to support groups. According to the American Psychiatric Association, whether to utilize CBT, an SRI, or combined treatment will depend on factors that include the nature and severity of the patient's symptoms, the nature of any co-occurring psychiatric and medical conditions and their treatments, the availability of CBT, and the patient's past treatment history, current medications, capacities, and preferences (American Psychiatric Association, 2007). The doses of the medications are higher than what is usually given in other anxiety or depressive disorders, and also the treatment lasts longer. If the first treatment attempt is unsuccessful, another drug or treatment option can be considered. It is important to be persistent and find the best treatment option for the patient.

9.1. Psychological Treatment

9.1.1. Cognitive-behavioural Therapy

Cognitive-behavioural therapy is the most effective evidence-based psychotherapy for OCD. It involves 2 components: cognitive reappraisal or restructuring and behavioural interventions, typically in the form of exposure and response prevention (ERP). The 2 components of CBT can be used either jointly or independently, although in practice, exposure-response prevention is the most frequently used approach (Hirschtritt et al., 2017). CBT has two general aims: controlling compulsive rituals and avoidance, and reducing the anxiety associated with obsessions, and through this, reducing their intensity and frequency. CBT alone is recommended as initial treatment for a patient who is not too depressed, anxious, or severely ill to cooperate with this treatment modality, or who prefers not to take medications and is willing to do the work that CBT requires. In one study, ERP was found to be superior to clomipramine and to a pill-placebo (Foa et al., 2005). Combined treatment, of CBT and pharmacotherapy, should be considered for patients with an unsatisfactory response to monotherapy, for those with co-occurring psychiatric conditions for which SSRIs are effective, and for those who wish to limit the duration of SSRI treatment. According to Foa, ERP combined with medication was also more efficacious than either medication alone (Foa et al., 2005). Literature also demonstrates that CBT is effective regardless of baseline symptom severity, symptom subtype, gender, number of sessions, or comorbidity profile (Olatunjiet al., 2013). However, there are some barriers to CBT treatment, including lack of availability (eg, few local clinicians, especially those trained in OCD-specific approaches), intense time requirements (typically 1 or more hours a week for therapy sessions, plus daily "homework" assignments during at least 12 weeks),and patient motivation to engage in CBT (Hirschtritt et al., 2017). Nonetheless, despite these barriers, no other psychosocial intervention has so consistently outperformed other treatment modalities.

9.1.1.1. Behavioural Treatment

Behavioural treatment was introduced in 1966 by Meyer, who described two patients successfully treated with a behavioural therapy program that included prolonged exposure to distressing objects and situations, combined with strict prevention of rituals (exposure and response prevention). Mayer continued to implement this treatment program with additional OCD patients, and found that it was highly successful in 10 of 15 cases, and partially effective in the remaining patients. Moreover, 5 years later, only two of the patients in the case series had relapsed (Meyer, 1974). The goal of exposure and response prevention is to break the cycle of conditioning that maintains the disorder. While the exact mechanisms of this treatment are unknown it is hypothesized that ERP for OCD is effective because of the resultant 1) cognitive change (correction of faulty assumptions); 2) habituation to the conditioned fear; or 3) increases in self-efficacy (Abramowitz, 2006). If exposure is done long enough and frequent enough, the patient's anxiety will decrease. However, for exposure to be effective patients must be prevented from performing rituals, otherwise they will use the rituals to manage their anxiety during exposure. The first step in exposure is to create a hierarchy of the patient's obsessive thoughts and situations that are avoided. These are then ranked from least anxiety-provoking to the most. The exposure exercises typically begin with the lowest-ranking item on the hierarchy in the presence of the therapist, either in the consulting room, in the form of imaginal exposure, or in an actual situation (that is, in vivo exposure). Throughout the exposure, the patient is asked to rate his or her anxiety, from 0 to 10, on the subjective units of distress scale (SUDS). Exposure is continued until the patients anxiety is reduced, ideally by at least half on the SUDS. At the end of each treatment session, the therapist instructs the patient to continue exposure for several hours alone and in different environmental contexts. After the first item on the hierarchy has been mastered, exposure to the next item is begun. Deciding between imaginal or in vivo exposure will depend upon the

patient's obsessions. If the patient has fears of committing some unacceptable action or some catastrophe (e.g., family member being killed), imaginal exposure should be performed. In this case, a scenario can be created in which the patient's fears come true. The session could be tape recorded so that the patient can listen to it repeatedly, in the session and at home, until their anxiety decreases on the SUDS. Other obsessions are most easily accessed with in vivo exposure. This is common when patients have a fear of contamination. In such cases the patient is put into contact with the feared situation (e.g., touching a doorknob) and then urged not to perform the compulsion or ritual (e.g., hand washing). This type of response prevention is key, and patients should be prevented from performing rituals not only during exposure session, but also throughout the day. It is common for patients to have some lapses in response prevention during treatment, and it is advised for the patient to continue to log all rituals. In some cases it may be helpful to involve family members so that they could remind the patients to forgo the rituals and also refuse to help and provide reassurance. One highly successful format for ERP comprises a few hours of assessment and treatment planning followed by 16 twice-weekly treatment sessions lasting about 90 to 120 minutes each and spaced over about 8 weeks (Abramowitz et al., 2003). In reviewing the results of more than 200 OCD patients treated with behaviour therapy in several countries, Foa et al. reported that 51 % of sufferers achieved at least a 70 % reduction in symptoms. Thirty-nine percent of patients achieved reductions ranging from 31 % to 69 %, and 10 % were considered failures, failure being defined as patients with an improvement of 30 % or less (Foa et al., 1985).

9.1.1.2. Cognitive Therapy

Cognitive therapy (CT) is designed to help patients identify their automatic unrealistic thoughts and change their interpretations of the meaning of the thoughts, thus ultimately leading to a decrease in anxiety and compulsions. In the first stage of CT, patients are taught

to develop an awareness of their worries as obsessions and their rituals as compulsions. They are instructed to keep a daily diary of obsessions, called a thought record, where they can write down their obsessions, any interpretations, what they were doing when the obsession began, and their response to the obsession. The therapist then reviews this record with the patient and addresses the interpretation of the obsessions. Using gentle reasoning and Socratic questioning, the therapist will verbally challenge an unrealistic belief. This helps the patient to identify the cognitive distortion, typically a faulty assessment of danger, an exaggerated sense of responsibility, or fears that thinking something negative will make it come true (thought-action fusion) (Foa, 2010). Once patients are able to quickly identify their obsessions and compulsions as symptoms of OCD, the therapist will initiate a few behavioural experiments to disprove errors in thinking about cause and effect. For example: if a patient believes that closing the door five times will prevent their family from being in a car crash, the therapist may instruct the patient to close the door four times and to see if any harm will come to their family. The results of this experiment could further be used to asses other unrealistic thoughts and over time patients will learn to independently identify and re-evaluate their faulty beliefs.

9.1.1.2.1. Danger Ideation Reduction Therapy

In practise explicitly cognitive techniques are used to challenge inflated responsibility, overestimation of threat, thought-action fusion, perfectionism and other maladaptive appraisals thought to maintain OCD. A novel cognitive intervention called Danger Ideation Reduction Therapy (DIRT) was evaluated in a pair of Australian studies (Jones and Menzies, 1998; Krochmalik et al., 2004). DIRT targets danger-related cognitions regarding contamination while avoiding any behavioural strategies. It is based on the rationale that the therapist should provide as much factual information as possible. DIRT consists of six discrete treatment components aimed at reducing the number of intrusive thoughts

experienced and concurrently allowing the patient to successfully change the remaining thoughts and beliefs. The treatment includes: attentional focusing, filmed interviews, corrective information, cognitive restructuring, expert testimony, microbiological experiments and a probability of catastrophe assessment task (Jones and Menzies, 1998). In the study conducted by Jones and Menzies, DIRT showed significantly greater reductions in symptomatology from pre-treatment to after treatment on all four outcome measures than subjects who did not receive DIRT (Jones and Menzies, 1998). The second study by Krochmalik et al., also confirmed the hypothesis that DIRT represents a viable alternative to the standard behavioural approach to OCD. Indeed, DIRT was not only associated with significant reductions in OCD symptomatology, it also outperformed ERP on the most widely used measures in the assessment of this disorder (Krochmalik et al., 2004).The fact that DIRT was superior to comparison conditions in two studies confirms its effectiveness for patients with the contamination/washing subtype of OCD.

9.1.2. The Future of CBT: Remote Treatment

Recent research has focused on improving dissemination of CBT with technology or internet based delivery. Using these technology aids the patient and the therapist interact in real-time without having to be face to face. Evidence from various studies suggests that remote CBT demonstrates efficacy similar to that of in-person treatment. Remote treatment does not require the patient to attend traditional face-to-face treatment services and is thus important for those individuals who avoid seeking treatment because of stigma or have a preference to self-manage symptoms. Furthermore, not only does this type of treatment reduce the therapist time that is required to treat the patients, but it also provides the potential for considerable cost savings to healthcare providers. Typical technologies that are used in remote treatment

include traditional or internet-based videoconferencing, the telephone, computerized CBT, and programs accessed via the internet.

9.1.2.1. Videoconferencing administered CBT (vCBT)

Videoconferencing delivered CBT involves the client and the therapist interacting via a video-link, thus the client's non-verbal behaviours are able to be observed. In one study conducted by Stubbings et al., CBT via videoconference was evaluated in the treatment of mood and anxiety disorders. The findings of this controlled trial indicated that CBT was effective in significantly reducing symptoms of depression, anxiety, and stress and increasing quality of life in both in-person and videoconferencing conditions, with no significant differences being observed between the two (Stubbings et al., 2013).

9.1.2.2. Telephone administered CBT (tCBT)

Telephone administered CBT interventions involve the client and therapist interacting over the telephone. Studies comparing tCBT with face-to-face CBT have emerged in both adolescent (Turner et al., 2014) and adult (Lovell et al., 2006) samples. Both studies demonstrate equivalent outcomes across methodologies and have found tCBT to be an effective treatment and not inferior to standard clinic-based CBT.

9.1.2.3. Computerized CBT (cCBT)

Computerized treatments are those that consist of a treatment program that is usually loaded on to a single computer or are administered via a computerized device. The most commonly used computerized program for the treatment of OCD is the Behaviour Therapy (BT) Steps program. Individuals access the computer generated program via a touch tone telephone rather

than a computer, and they advance through each of the steps at their own pace (Wootton, 2013). In the study conducted by Greist et al., 218 OCD patients at 8 North American sites were randomly assigned to 10 weeks of behaviour therapy treatment guided by either a computer accessed by telephone and a user workbook, a behaviour therapist, or systematic relaxation guided by an audiotape and manual. The results showed that by week 10, the mean change in score on the Y-BOCS was significantly greater in clinician-guided behaviour therapy (8.0) than in computer-guided (5.6), and changes in scores with both clinician-guided and computer-guided behaviour therapy were significantly greater than with relaxation (1.7), which was ineffective (Greist et al. 2002). Therefore although computer-guided behaviour therapy was effective, clinician-guided behaviour therapy was shown to be even more effective.

9.1.2.4. Internet-administered CBT (iCBT)

Internet-delivered treatments are those that have materials that are accessible via the internet and are thus generally more flexible than computerized treatments. iCBT can be delivered as open access programs (where anyone can access the program) or can be closed (where the patient logs in with a secure username and password).

9.1.2.5. Bibliotherapy administered CBT (bCBT)

Bibliotherapy is a remote treatment where the individual is provided with a printed workbook to conduct his or her own treatment. It involves teaching the individual the same skills and techniques taught in face-to-face treatment, however, material is presented in a paper workbook rather than online or via a computer

9.2. Biological Treatment

9.2.1. Pharmacotherapy

9.2.1.1. Selective Serotonin Reuptake Inhibitors

Serotonin (5-hydroxytryptamine, 5-HT) is a neurotransmitter that influences multiple processes, including autonomic function, motor activity, hormone secretion, cognition, and complex processes associated with affection, emotion, and reward. SSRIs are believed to increase the extracellular level of the neurotransmitter serotonin by limiting its reabsorption into the presynaptic cell. The molecular target for SSRIs is the solute carrier family 6 (neurotransmitter transporter, serotonin), member 4 (SCL6A4). It is responsible for terminating the action of 5-HT in the synaptic cleft (Sangkuhl et al., 2009). Released serotonin is transported back into the presynaptic terminals via this integral membrane protein. SSRIs compose first-line pharmacologic treatment for OCD. Clinical practice guidelines suggest that optimal treatment for OCD involves using SSRIs at the maximal tolerated dose within the Food and Drug Administration dosing guidelines for at least 8 to 12 weeks. Further evidence suggests that continuing SSRI medications for at least 6 to 12 months after response to treatment is advisable; withdrawing SSRIs at any point is likely associated with a significant risk of relapse (Hirschtritt et al., 2017). SSRIs are well absorbed from the gut and are primarily metabolized via hepatic route. They are associated with numerous drug interactions; most notably with MAO inhibitors. The combination of SSRIs and MAO inhibitors may trigger serotonin syndrome. Although the efficacy of the SSRIs is comparable to that of the tricyclic antidepressants (TCA), the SSRIs have significantly fewer side effects. They do not cause cardiac conduction abnormalities in overdose, are associated with fewer antimuscarinic side effects, and have low propensity to cause seizures. Gastrointestinal disturbances, such as nausea and diarrhea, usually occur at the beginning of treatment and

subside after the first week. Other adverse effects include: insomnia, sexual dysfunction, increased risk of bleeding (when taken with anticoagulation drugs), suicidal ideation, and serotonin syndrome with overdose. Because of their wide therapeutic index, most patients will have mild or no symptoms following moderate overdoses and rarely deaths occur.

9.2.1.1.1. Fluoxetine (Prozac®, Fluval®, Portal®)

The recommended dosage for adults is 20 mg daily. However, if after 2 weeks of treatment there is no significant improvement in OCD symptoms the dosage can be raised to a maximum of 60 mg. The efficacy of fluoxetine at three fixed doses (20, 40, and 60 mg) was examined in a multicenter trial by Tollefson et al., who reported symptom reduction of 32.1%, 32.4%, and 35.1%, respectivey, as compared with 8.5% for placebo after a 13 week trial (Tollefson et al., 1994). In children (> 8 years old) and adolescents the starting dose is 10 mg, and the maximum daily dose is 20 mg.

9.2.1.1.2. Escitalopram (Cipralex®, Citram®, Elicea®, Escital®, Zepira®, Serpentil®)

The beginning dosage for adults is 10 mg once a day. Depending on the effects it has on the patient, the dosage could be increased to a maximum of 20 mg per day. Escitalopram discontinuation, particularly abruptly, may cause certain withdrawal symptoms such as electric shock sensations, dizziness, acute depressions and irritability, as well as heightened senses of akathisia. When discontinuing medication, the dosage should be decreased gradually through the course of two weeks in order the reduce withdrawal symptoms.

9.2.1.1.3. Sertraline (Zoloft®, Halea®, Luxeta®, Sonalia®)

The recommended starting dosage for adults is 50 mg daily; with a maintanence dose of 50-200 mg once a day. In children aged 6-12 the starting dose is 25 mg, while those aged 13-17 it is also 50 mg. Maintenance dose ranges from 25-200 mg for children aged 6-12, while those aged 13-17 follow the same maintenance dosage as adult. A large multicenter placebo controlled trial of fixed-dose sertraline (50, 100, 200 mg) found that doses of 50 mg and 200 mg were significantly more effective than placebo in reducing obsessional symptoms (Greist et al., 1995).

9.2.1.1.4. Paroxetine (Paroxin®, Seroxat®)

The target dose is 40 mg once a day. Treatment begins with a daily dose of 20 mg, which is then increased for 10 mg increments at weekly intervals, according to clinical response and tolerability. Paroxetine has also been reported to be more effective than placebo in a multicenter trial but only at doses of 40 mg and 60 mg per day, with 20 mg being no different from placebo (Hollander et al., 2000). Paroxetine may increase the risk of suicidal thinking and behaviour in children and adolescents and should thus be avoided in this age group.

9.2.1.1.5. Fluvoxamine (Fevarin®, Floxyfral®, Dumyrox®, Luvox®)

The initial dose is 50 mg daily. This is then increased by 25 mg every 4-7 days until the maintenance dose of 100-300 mg is achieved. The FDA has added a black box warning for this drug in reference to increased risks of suicidal thoughts and behaviour in young adults and children. Fluvoxamine is not approved for use in all children.

9.2.1.2. Clomipramine (Anafranil®)

Clomipramine is a tricyclic antidepressant that was discovered in 1964 and it is still being used today. The maximal daily dosage for adults is 250 mg, while for children it is 200 mg. It is a highly selective inhibitor of serotonin reuptake. It is also an antagonist/inverse agonist at the histamine H1 receptor, the muscarinic acetylcholine receptors and the α1 adrenergic receptor. These last three actions likely contribute to its adverse effects. Specifically, clomipramine has substantial anticholinergic effects, such as dry mouth, blurred vision, constipation, fatigue, tremor, and hyperhidrosis. Furthermore, clomipramine is associated with increased risk of arrhythmia and seizures at doses greater than 200 mg daily, thus requiring monitoring of serum concentration. Thus, clomipramine is most appropriate as a second-line treatment for patients who do not respond to SSRIs.

9.2.1.3. Other Medication

In the case of ineffective treatment with SSRIs or TCA, the following drugs can be added to therapy: Valproate (Depakine®), Lithium, or Carabamazepine (Tegretol®).

9.2.2. Electroconvulsive Therapy

Electroconvulsive therapy (ECT) is not currently used as a first-line treatment for obsessive-compulsive disorder (OCD). However, several studies have reported its effectiveness in treating severe OCD, especially when first line therapies have failed. In one study by Liu Xiaohui et al., three patients with severe OCD were treated by modified bifrontal ECT after their first-line anti-OCD treatments (pharmacotherapy, behavioral therapy, and cognitive behavioral therapy) failed. The resultls showed that in all three cases, the patients' depressive symptoms improved considerably after the ECT procedures (Liu Xiaohui et al., 2014).

9.2.3. Surgical Treatment

Surgery for OCD is reserved for patients with the most severe cases of the disease, refractory to pharmacotherapy and psychotherapy. To be referred to surgery, certain requirements must be met; the patient must have had adequate trials (at least 10 weeks at maximally tolerated dose) of clomipramine, fluoxetine, fluvoxamine, sertraline, paroxetine, and a monoamine oxidase inhibitor. Also all patients must have had extended trial of behaviour therapy consisting of a minimum of 20 hours of ERP (Jenike et al., 1998). Contraindications must also be taken into consideration such as: age below 18 or above 65, inability to comply with treatment, and previous diagnosis or neurosurgical procedure. Two methods of surgery are currently employed: one involves performing a lesion, and the other involves stimulation of target areas using deep brain stimulation (DBS). In a lesion, a radiofrequency unit is used to produce a thermal lesion of calculated volume. This is permanent and irreversible. In DBS an electrode is implanted at the site of the target and current is delivered through a pacemaker to alter the signals emanating from the target. Both this procedures are performed using stereotactic techniques which offer a high degree of accuracy (within 1-2mm) (Doshi, 2009). The four procedures currently being used are: anterior capsulotomy, cingulotomy, subcaudate tractotomy and limbic leucotomy. Unfortunately there have been few comparison studies of these operations, so no single procedure is classified as the best. The most commonly performed surgical procedure is bilateral cingulotomy. In one study by Jung et al., the Y-BOCS fell by 48% (Jung et al., 2006). Some patients with only limited response to surgery report better response to pharmacotherapy and behavioural therapy post operatively (Spofford et al., 2014). The most common complications following surgery include: infection, haemorrhage, epileptic seizures, and weight gain. Some countries have abandoned neurosurgery altogether, while in others it is only used in a few centers.

9.3. Social Therapy

Social therapy is a particular kind of group therapy. The group consists of people of various backgrounds, histories and ages. While traditional therapies typically focus on the individual, social therapy focuses on the group and on being with others to grow and develop emotionally.

9.3.1. Work Therapy

Work therapy is an excellent type of therapy that offers patients an opportunity to be productive. Patients work together to accomplish various goals that are clearly outlined to them in the beginning of the sessions. An activity program with adequate leadership and personnel is established. Activities range from food preparation, landscaping, dressmaking, carpentry etc…

9.3.2. Art Therapy

Art therapy is a prospective outlet for people who don't know how to verbalize their feelings during traditional psychotherapy sessions. It allows patients to set goals and create in a safe space under the supervision of a professional. Various techniques are used such as painting, drawing, sculpting or other types of artwork.

10. COURSE AND PROGNOSIS

In more than half of patients, OCD begins with an abrupt appearance of symptoms. The first symptoms usually begin after some stressful life event, such as the death of a loved one. Diagnosis is not made right away since the majority of patients successfully hide their disorder, especially those with the milder form. OCD is usually a chronic disorder with a fluctuating course in most of patients. A study conducted by Rasmussen and Eisen in 1992 reported that 85 % of OCD patients had a continuous fluctuating course, 10 % had a deteriorative course and 2 % were classified as episodic (Rasmussen and Eisen., 1992). More recently in 1999, Skoog and Skoog, in a 40 to 50 year follow up of OCD patients, found that overall clinical and subclinical symptoms were still evident in two-thirds of the sample at follow-up, and 10 % of the sample showed a deteriorating course (Skoog and Skoog, 1999). The majority of patients have both obsessions and compulsions as well as comorbidity with other psychiatric disorders. Long-term complications of OCD have to do with the type of obsessions or compulsions. For example, constant handwashing can cause skin breakdown. OCD does not usually progress into another mental problem. Complete recovery to the point of no longer requiring treatment is considered uncommon. However, if proper treatment is started OCD can be managed and controlled and the patient can have an excellent quality of life.

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12. REFERENCES

1. Abramowitz, J.S. (2006). The psychological treatment of obsessive–compulsive disorder. Canadian Journal of Psychiatry, 51(7), 407–416.

2. Abramowitz JS, Foa EB, Franklin ME. (2003). Exposure and ritual prevention for obsessive-compulsive disorder: effects of intensive versus twice-weekly sessions. J Consult Clin Psychol 2003;71:394–8.

3. Aouizerate, B., Guehl, D., Cuny, E., Rougier, A., Burbaud, P., Tignol, J., & Bioulac, B. (2005). Updated overview of the putative role of the serotoninergic system in obsessive-compulsive disorder. Neuropsychiatric Disease and Treatment, 1(3), 231–243.

4. Browne, H. A., Gair, S. L., Scharf, J. M., & Grice, D. E. (2014). Genetics of Obsessive-Compulsive Disorder and Related Disorders. The Psychiatric Clinics of North America, 37(3), 319–335.

5. Chakrabarty K, Bhattacharyya S, Christopher R, Khanna S. (2005). Glutamatergic dysfunction in OCD. Neuropsychopharmacology 30:1735–1740.

6. Diagnostic and statistical manual of mental disorders: DSM-5. (2013). Washington, Londres: American Psychiatric Association.

7. Doshi, P. K. (2009). Surgical treatment of obsessive compulsive disorders: Current status. Indian Journal of Psychiatry, 51(3), 216–221.

8. Foa, E. B. (2010). Cognitive behavioral therapy of obsessive-compulsive disorder. Dialogues in Clinical Neuroscience, 12(2), 199–207.

9. Foa EB, Liebowitz MR, Kozak MJ, Davies S, Campeas R, Franklin ME. (2005). Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. American Journal of Psychiatry. 2005;162:151–161.

10. Foa EB, Steketee GS, Ozarow BJ. (1985). Behaviour therapy with obsessive compulsives: from therpy to treatment. In Mavissakalian M,Turner SM, Michelsen L (Eds), Obsessive Compulsive Disorder: Psychological and Pharmacological Treatment. New York: Plenum Press.

11. Greist J, Chouinard G, DuBoff E, Halaris A, Kim SW, Koran L, Liebowitz M, Lydiard RB, Rasmussen S, White K, Sikes C. (1995). Double blind parallel comparison of three doses of sertraline and placebo in outpatients with obsessive compulsive disorder. Archives of General Psychiatry, 52, 29-95.

12. Greist, J.H., Marks, I.M., Baer, L., Kobak, K.A., Wenzel, K.W., Hirsch, M.J., & Clary, C.M. (2002). Behavior therapy for obsessive–compulsive disorder guided by a computer or by a clinician compared with relaxation as a control. Journal of Clinical

13. Grimshaw L. (1964). Obsessional disorder and neurological illness, J Neurol Neurosurg Psychiatry 27:229.

14. Hirschtritt ME, Bloch MH, Mathews CA. (2017). Obsessive-Compulsive Disorder Advances in Diagnosis and Treatment. JAMA. 2017;317(13):1358-1367.

15. Hollander E, Kaplan A, Allen A, Cartwright C. (2000). Pharmacotherapy for obsessive-compulsive disorder. Psychiatric Clinic of North America, 23, 643-56).

16. Jenike, Michael A., Lee Baer, and William E. Minichiello. (1998). Obsessive-compulsive disorders: practical management. St. Louis: Mosby.

17. Jones, M. K., & Menzies, R. G. (1998a). Danger Ideation Reduction Therapy (DIRT) for obsessive-compulsive washers. A controlled trial. Behaviour Research and Therapy, 36, 959-970.

18. Jung HH, Kim CH, Chang JH, Park YG, Chung SS, Chang JW. (2006) Bilateral anterior cingulotomy for refractory obsessive-compulsivedisorder: Long-termfollow-up results. Stereotact Funct Neurosurg 84(4): 184-9.

19. Kolada, J.L., Bland, R.C. and Newman, S.C. (1994), Obsessive-Compulsive Disorder. Acta Psychiatrica Scandinavica, 89: 24–35.

20. Krochmalik A, Jones MK, Menzies RG, Kirkby K. The superiority of danger ideation reduction therapy (DIRT) over exposure and response prevention (ERP) in treating compulsive washing. Behaviour Change. 2004;21:251–268

21. Leahy, R. L., McGinn, L. K., & Holland, S. J. (2012). Treatment plans and interventions for depression and anxiety disorders. New York: Guilford Press.

22. Liu, X., Cui, H., Wei, Q., Wang, Y., Wang, K., Wang, C., … Xie, X. (2014). Electroconvulsive Therapy on Severe Obsessive-Compulsive Disorder Comorbid Depressive Symptoms. Psychiatry Investigation, 11(2), 210–213.

23. Lovell, K., Cox, D., Haddock, G., Jones, C., Raines, D., Garvey, R., Hadley, S. (2006). Telephone administered cognitive behaviour therapy for treatment of obsessive compulsive disorder: randomised controlled non-inferiority trial. BMJ□: British Medical Journal, 333(7574), 883.

24. Meyer V, Levy R, Schnurer A. (1974). A behavioral treatment of obsessive-compulsive disorders. In Beech HR, ed. Obsessional states. London, UK: Methuen.

25. Olatunji, B.O., Davis, M.L., Powers, M.B., & Smits, J.A.J. (2013). Cognitive–behavioral therapy for obsessive–compulsive disorder: A meta-analysis of treatment outcome and moderators. Journal of Psychiatric Research, 47(1), 33–41.

26. Pitman RK. (1982). Neurological etiology of obsessive-compulsive disorders. Am J Psychiatry 139:139-140.

27. Practice Guidelines for the Treatment of Patients With Obsessive-Compulsive Disorder, American Psychiatric Association (2007)

28. Rapoport JL. (1989). The biology of obsessions and compulsions, Sci Am March:83-89.

29. Rasmussen SA, Eisen JL. (1992). The epidemiology and clinical features of obsessive-compulsive disorder. Psychiatric Clinics of North America,15, 743-58.

30. Rasmussen SA, Eisen JL. (1992). The Epidemiology and Differential Diagnosis of Obsessive Compulsive Disorder. J. Clin. Psychiatry 53(4):3-9.

31. Salkovskis, P.M., & Kirk, J. (1989). Obsessional disorders. In K. Hawton, P.M. Salkovskis, J. Kirk, & D. M. Clark (Eds.), Cognitive behavioural therapy for psychiatric problems: A practical guide (pp. 179-208). Oxford: Oxford University Press.

32. Stefan Kempke and Patrick Luyten (2007). Psychodynamic and cognitive–behavioral approaches of obsessive–compulsive disorder: Is it time to work through our ambivalence? Bulletin of the Menninger Clinic: Vol. 71, December, pp. 291-311.

33. Stein, Dan J., Eric Hollander, and Barbara Olasov. Rothbaum. (2010). Textbook of anxiety disorders. Washington, DC: American Psychiatric Pub.

34. Salkovskis, P.M., & Kirk, J. (1997). Obsessive-compulsive disorder. In D. M. Clark & C. G. Fairburn (Eds), Science and Practice of cognitive behaviour therapy (pp. 179-208). Oxford: Oxford University Press.

35. Sangkuhl, K., Klein, T., & Altman, R. (2009). Selective Serotonin Reuptake Inhibitors (SSRI) Pathway. Pharmacogenetics and Genomics, 19(11), 907–909.

36. Skoog G, Skoog I. (1999) A 40 year follow-up of patients with obsessive-compulsive disorder. Archives of General Psychiatry, 56, 121-7.

37. Soiffird CM, McLaughin NC, Penzel F, Rasmussen SA, Greenberg BD. (2014). OCD behaviour therapy before and after gamma ventral capsulotomy: case report. Neurocase 20(1):42-5.

38. Stubbings, D. R., Rees, C. S., Roberts, L. D., & Kane, R. T. (2013). Comparing In-Person to Videoconference-Based Cognitive Behavioral Therapy for Mood and Anxiety Disorders: Randomized Controlled Trial. Journal of Medical Internet Research, 15(11), e258.

39. Tollefson GD, Birkett M, Kotan L, Genduso L. (1994) Continuation treatment of OCD: double blind and open label experience with fluoxetine. Journal of Clinical Psychiatry, 55 (10, Suppl.), 69-76.

40. Turner, C. M., Mataix-Cols, D., Lovell, K., Krebs, G., Lang, K., Byford, S., & Heyman, I. (2014). Telephone Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Non-inferiority Trial. Journal of the American Academy of Child and Adolescent Psychiatry, 53(12), 1298–1307.e2.

41. Whalen PJ, Kapp BS. (1991). Contributions of the amygdaloid central nucleus to the modulation of the nictitating membrane reflex in the rabbit, Behav Neurosci 105:141-153.

42. Wootton BM, Dear BF, Johnston L, Terides MD, Titov N. (2013). Remote treatment of obsessive-compulsive disorder: A randomized controlled trial. J Obsessive Compuls Relat Disord 2: 375–384.

43. URL-1: Stanford Medicine: Obsessive Compulsive and Related Disorders - Epidemiology, http://ocd.stanford.edu/about/prevalence.html

44. URL-2: Stanford Medicine: Obsessive Compulsive and Related Disorders – Diagnosis, http://ocd.stanford.edu/about/diagnosis.html

13. BIOGRAPHY

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