

Review

A Review of Behavioral and Pharmacological Treatments for Adult Trichotillomania

Lauren Parris Bennett ^{1,*} and Rebecca Ryznar ^{2,3}

¹ College of Osteopathic Medicine, Rocky Vista University, 8401 S Chambers Rd., Englewood, CO 80112, USA

² Department of Biomedical Sciences, Rocky Vista University, 8401 S Chambers Rd., Englewood, CO 80112, USA; rryznar@rvu.edu

³ Department of Tracks and Special Programs, Rocky Vista University, 8401 S Chambers Rd., Englewood, CO 80112, USA

* Correspondence: lauren.bennett@rvu.edu

Abstract: Trichotillomania (TTM) is a psychiatric disorder involving chronic, recurrent urges to pull out one's own hair, arising frequently in childhood and early adolescence. This disorder predominantly affects women and has a high co-morbidity with many other psychiatric conditions. Currently, the etiology is unknown, which makes treating TTM extremely difficult. While the epidemiology and proposed causes will be discussed briefly, the primary purpose of this review is to provide a comprehensive, updated summary of the psychological and pharmacological management options for patients diagnosed with TTM, as new clinical trial data for previously studied and novel treatments have become available within the last decade. Of the behavioral interventions, cognitive behavioral therapy (CBT) and habit reversal training (HRT) have demonstrated the greatest improvements in hair-pulling severity, with HRT showing the most efficacy for long-term maintenance of progress. Pharmacological therapies with the most success include Olanzapine, Clomipramine, and N-Acetylcysteine, though larger replication studies are needed. Selective serotonin reuptake inhibitors (SSRIs) have yielded inconsistent results in clinical trials, yet they are frequently prescribed for TTM. Naltrexone, Dronabinol, and Inositol are emerging as potential treatments, but the results suggest that additional studies are needed. Future research directions include larger placebo-controlled pharmacological trials, exploring the efficacy of combined behavioral and pharmacological approaches compared to monotherapy, and delving into the potential genetic and neurochemical contributions that may underlie TTM.

Keywords: hair-pulling disorder; body focused repetitive behavior; obsessive–compulsive disorder; habit-reversal training; cognitive behavioral therapy; n-acetylcysteine; antipsychotics



Citation: Bennett, L.P.; Ryznar, R.

A Review of Behavioral and Pharmacological Treatments for Adult Trichotillomania. *Psychol. Int.* **2024**, *6*, 509–530. <https://doi.org/10.3390/psycholint6020031>

Academic Editor: Mosad Zineldin

Received: 6 March 2024

Revised: 5 April 2024

Accepted: 10 April 2024

Published: 16 April 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Background

Trichotillomania (TTM), also called hair-pulling disorder, is a psychiatric disorder involving recurrent urges to pull out one's own hair, resulting in noticeable hair loss [1]. Though this condition has been described in medical literature since the 19th century, it was not added to the Diagnostic and Statistical Manual of Mental Disorders (DSM) until 1987 [1]. Trichotillomania is currently classified under Obsessive–Compulsive and other related disorders in the 5th edition of the DSM (DSM-5), a relatively recent change from its prior categorization under Impulse Control Disorders in the DSM-4 [2]. It is also considered a body-focused repetitive behavior (BFRB), along with nail-biting and skin-picking [3]. DSM-5 diagnostic criteria for trichotillomania include repeatedly pulling out one's own hair, resulting in hair loss, repeated attempts to decrease or stop hair-pulling, the hair-pulling causes clinically significant distress or impairment in social, occupational, or other important areas of functioning, the hair-pulling or hair loss is not attributable to another medical condition, and the hair-pulling is not better explained by symptoms of another mental disorder [4]. Additional clinical characteristics include feeling tension

before pulling, experiencing pleasure or relief after the hair is pulled, and playing with, chewing, biting, or eating the pulled hairs [1,3]. Common pulling sites include the scalp, eyebrows, eyelashes, pubic region, and extremities. TTM sufferers often experience shame, embarrassment, guilt, and low self-esteem, leading to self-isolation, among other negative impacts on quality of life [2]. Sufferers who have noticeable hair loss may purchase wigs or take other measures to conceal their hair loss, adding potential financial as well as emotional strain. Unfortunately, these social and psychological impairments can serve as a catalyst for subsequent hair-pulling episodes, illustrating the vicious cycle that this disorder takes on. Furthermore, these same feelings of shame and guilt may impede the individual from seeking help from medical professionals [2].

While hypothesized to be attributed to anxiety, stressful life events, neurochemical imbalances, genetic polymorphisms, or a combination of some or all of these factors, the etiology of trichotillomania ultimately remains unknown, which makes devising treatment plans difficult for clinicians and frustrating for patients [1,2]. While the proposed etiologies of this disorder will be briefly discussed in the preceding sections, the primary purpose of this review is to provide a comprehensive summary of psychological and pharmacological management options by examining studies conducted in adults. Given that new clinical trial data for previously studied and novel treatment approaches have become available within the last decade, we aim to communicate these new findings so that clinicians can make evidence-based decisions when selecting treatment options for their patients. Lastly, we will discuss clinical recommendations in the context of the data presented and offer directions for future research based on the knowledge gaps identified in the literature.

Epidemiology

The estimated prevalence of TTM is between 0.5 and 3% of the population [1]. Onset is typically between late childhood and early adolescence, with the condition often persisting into adulthood if not addressed promptly [1]. While this disorder has a relatively even distribution between males and females in the pediatric population, there is a striking female-to-male predominance of four to one in the general adult population [1,2]. It should be noted that many individuals with this disorder feel ashamed or embarrassed about their behavior and the resultant hair loss. The prevalence may be underestimated due to stigma, leading to underreporting of the condition [1]. TTM has a well-established, high co-morbidity with several other psychiatric disorders, with some studies estimating that nearly 80% of those diagnosed with TTM will be diagnosed with another psychological disorder in their lifetime [5,6]. The most common co-occurring disorders across studies are anxiety disorders (29–55%), depression (22–45%), attention deficit hyperactivity disorder (ADHD) (15–29%), post-traumatic stress disorder (PTSD) (19–29%), obsessive-compulsive disorder (OCD) (19–29%), skin-picking disorder (19–24%), and substance use disorder (15–19%) [1,5,7–10]. Additionally, up to 20% of people with TTM eat the hair they pull (trichophagia) [1]. This may result in the formation of gastrointestinal hairballs (trichobezoars), which have the potential to cause obstruction, warranting surgical intervention [1,11].

2. Proposed Causes

2.1. Genetic

Given that many of the co-occurring disorders have established genetic underpinnings, it is plausible that genetic contributions may underlie TTM as well [11]. One study by Hemmings et al. in 2006 explored the role that certain serotonergic and dopaminergic gene polymorphisms may play in the development of TTM by comparing gene variants between TTM, OCD, and control groups. Two of the genes explored are *5-HT2A* and *5-HTT*, coding for the 5-HT2A serotonin receptor and 5-HTT serotonin transporter, respectively [12]. Serotonin is involved in numerous CNS functions, including cognition, memory, social interactions, appetite, sexual behavior, and mood regulation [13,14]. *5-HT2A* gene mutations causing altered functioning of the 5-HT2A serotonin receptor result in impaired serotonin signaling in the CNS and have been implicated in depressive disorder

ders, obsessive–compulsive disorders, and schizophrenia [13,14]. Meanwhile, the 5-HTT serotonin transporter facilitates the re-uptake of serotonin from the synaptic space to the pre-synaptic neuron [12]. Mutations in the gene coding for the 5-HTT transporter are associated with increased transporter function and decreased serotonin availability, which is thought to increase the risk of developing certain anxiety and depressive disorders, as well as impulsivity and a heightened stress response [15,16]. Hemmings’ results demonstrated that while there were no significant differences in 5-HTT gene polymorphisms between groups, significantly more TTM patients possessed the T102C variant of the 5-HT2A gene when compared to both control and OCD groups, potentially linking TTM to dysfunction within the serotonergic neurotransmitter system [12].

The same study also explored two dopaminergic genes, *DRD1* and *DRD4*, which encode the D1 and D4 dopamine receptor subtypes, respectively [12]. In the CNS, this neurotransmitter system regulates various motor functions and strengthens neural reward pathways [16]. Gene mutations leading to dopamine dysregulation could potentially contribute to the rewarding or pleasurable sensation experienced by those with TTM when a hair is pulled. While Hemmings and colleagues found no association between *DRD1* and *DRD4* variants and TTM, other studies have correlated mutations in these genes with impulsivity, novelty-seeking behavior, reward deficiency, and a higher propensity for the development of ADHD [12]. Furthermore, prior studies of animal models demonstrated that *DRD1* gene variants are associated with abnormal grooming behavior in rodents [17,18]. Other rodent studies have found that deletions in the *SAPAP3* gene, whose protein forms a scaffolding complex at post-synaptic glutamatergic synapses, are associated with excessive grooming behavior [19]. A subsequent study exploring this gene in humans found that four specific polymorphisms of the *SAPAP3* gene had statistically significant associations with at least one grooming disorder (skin picking, nail biting, or trichotillomania) [19]. A summary of these genes, their functions, and potential implications for TTM is depicted in Figure 1.

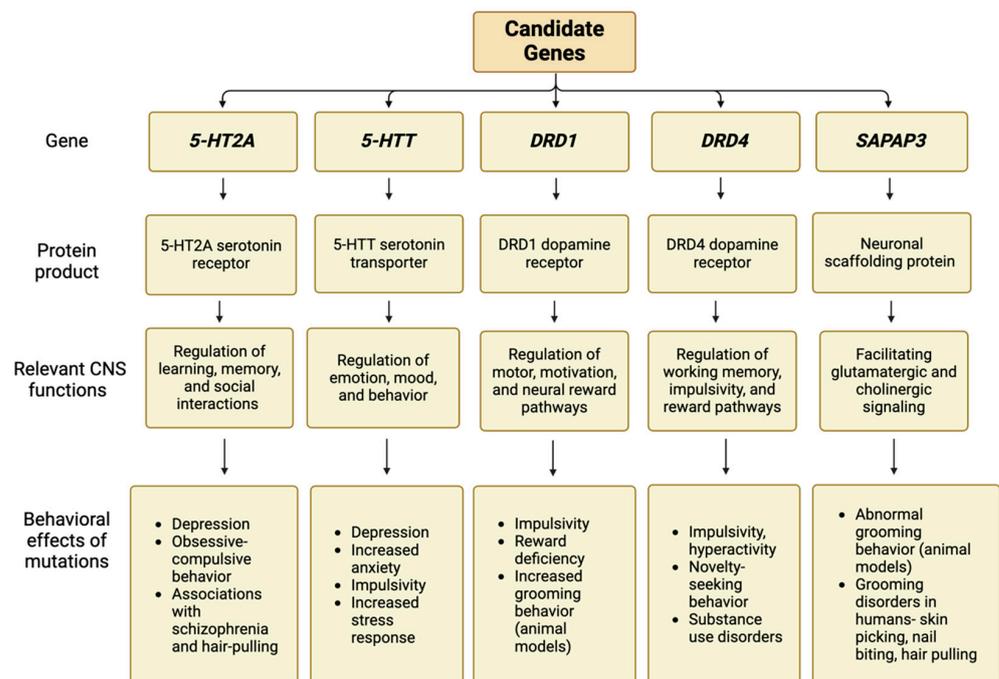


Figure 1. Candidate genes explored for genetic correlates of trichotillomania: relevant CNS functions and implicated behavioral changes associated with mutations. This image was created using Biorender (<https://www.biorender.com>).

2.2. Neurobiological

Magnetic resonance imaging (MRI) studies exploring brain regions involved in motor control and motor learning suggest that TTM could be associated with structural cerebral anomalies, particularly in regions of the brain that regulate motor and executive functions. One small study by O'Sullivan et al. demonstrated that left putamen volumes were significantly smaller in ten subjects with TTM compared to ten controls [20]. One of the structures comprising the basal ganglia, the putamen, is involved with motor learning, motor control, reward, and addiction [21]. A similarly designed study by Keuthen et al. explored the cerebellum as a potential region implicated in TTM development, as this structure modulates descending motor pathways to fine-tune movement and aid in coordinating voluntary movement [22]. Indeed, this study demonstrated significantly smaller volumes in subjects with TTM when compared to controls, with the severity of symptoms inversely correlated with cerebellar volume [23]. Yet another small study of ten TTM patients demonstrated volume reductions in the left inferior frontal gyrus compared to ten healthy controls [24]. This brain region is involved in executive functions, including self-control [24]. Other studies have not only explored the role of specific brain regions but also neural circuits *between* brain regions. Studies in the early 2000s demonstrated that TTM patients display reduced integrity of white matter tracts between bilateral anterior cingulate cortices and orbitofrontal cortices, responsible for reward-guided decision making and impulse control plus response inhibition, respectively [25,26]. Other research has explored functional impairment as it correlates to symptom severity. One study by Chamberlain et al. in 2006 demonstrated that TTM patients display impaired motor response inhibition compared to healthy controls, with deficits positively correlating with symptom severity [26]. A 2015 study by Flessner and colleagues similarly explored the relationship between executive functioning and the severity of symptoms in people exhibiting BFRBs compared to healthy controls. TTM, nail biting, and skin picking were examined in this study. The executive function was assessed by having subjects perform tasks in cognitive flexibility, spatial planning, and working memory. A significant difference was found between groups during cognitive flexibility tasks, with the BFRB group demonstrating more errors than the controls [27]. Though each of these aforementioned studies comprised small subject pools, they nonetheless demonstrate an intriguing trend of people with TTM displaying structural anomalies in brain areas regulating motor function, decision-making, and impulse control.

2.3. Environmental

Other studies propose that TTM could arise after experiencing significant stressors, particularly during childhood. Some proposed stressors include death, injury, or illness of a family member; separation from friends or family members; parental divorce; physical abuse; or sexual abuse [28]. One hypothesis is that stress triggers the onset of the disorder, with hair-pulling serving as a responsive, self-soothing behavior [3,28]. One study from the early 2000s interviewed a group of women ($n = 44$) with the disorder. Researchers found that 91% of subjects had experienced some form of trauma, violence, or abuse in their lifetime. These events included repetitive psychological, physical, or sexual abuse by family members, strangers, or acquaintances [29]. Notably, 86% of participants reported these horrific events concurrent with the onset of their disorder [29]. Another study from 2013 published in the *Journal of Obsessive–Compulsive and Related Disorders* examined the influence of family dynamics on the development of TTM. In a comparison of 49 teens with TTM to 23 controls, it was found that the TTM group reported more conflict and aggression amongst family members, as well as less familial support, when compared to the control group [30]. Though both studies had relatively small sample sizes, they still present a notable correlation between interpersonal or family turmoil and the development of trichotillomania.

3. Review Methodology

A literature search in the databases PubMed, MEDLINE Complete, Google Scholar, and the Psychological and Behavioral Sciences Collection was conducted from January 2022 to May 2022. The following search criteria were used in each database: “(Trichotillomania OR Hair Pulling Disorder) AND (behavioral treatment OR behavioral intervention)”. An identical approach was used for pharmacological interventions with the search criteria “(Trichotillomania OR Hair Pulling Disorder) AND (pharmacological treatment OR pharmacological intervention)”. We limited the search to abstracts or full-text articles available in English. Only studies with adult populations (age 18 or older) were included. Additionally, we excluded studies where the given intervention was intended to treat another condition, such as nail biting. We also excluded studies that intended to treat a combination of conditions, such as treatment of TTM and Tourette syndrome. After applying these criteria and eliminating duplicates, animal studies, review articles, and editorials, a total of 44 studies were selected for this review.

4. Treatment Approaches

The current treatment recommendations for TTM fall into two broad categories: behavioral and pharmacological. The following sub-sections discuss each approach and summarize study findings per treatment modality. Additionally, various clinical scales assessing TTM impairment, severity, and improvement are utilized in these studies as primary outcomes and will be referenced in the subsequent sections. Detailed descriptions of these clinical scales can be found in Appendix A.

4.1. Cognitive Behavioral Therapy (CBT)

CBT is a form of psychotherapy in which an individual identifies unhelpful or destructive thoughts and behaviors and then makes a deliberate effort to reevaluate and change their thinking patterns and actions [31]. Of the CBT studies conducted in adults with TTM, some have compared this technique with a pharmaceutical agent and placebo or waitlist control. Two parallel treatment studies compared CBT with either the tricyclic antidepressant, Clomipramine, or the selective serotonin reuptake inhibitor, Fluoxetine, with a placebo group. Both studies found that CBT was statistically more effective at reducing hair-pulling severity as assessed by the Massachusetts General Hospital Hair-Pulling Scale (MGH-HPS) when compared to both drug and placebo groups [32,33]. Other studies have compared CBT to other behavioral interventions, including supportive therapy and behavior therapy [34,35]. In these studies, the CBT group had lower (improved) MGH-HPS scores after treatment compared to pre-treatment baseline scores. Another study compared CBT to cognitive bias training *plus* CBT [36]. Lastly, one study analyzed six individuals who received an intensive, three-day CBT intervention in a group therapy setting [37]. Subjects in these two studies saw overall lower MGH-HPS scores in those who received CBT [36,37]. Three of the aforementioned studies also conducted follow-up assessments at various timepoints, from three months to two years after CBT intervention [35–37]. A common finding was that while CBT showed a significant reduction in hair-pulling immediately upon intervention completion, nearly all subjects' MGH-HPS scores worsened, some back to baseline, when re-assessed at the follow-up timepoints [35–37].

4.2. Habit Reversal Training (HRT)

HRT is a subset of CBT that involves three components. The first is awareness training, where an individual makes a conscious effort to observe the circumstances under which they pull [38]. Second is competing response training, where the individual substitutes another behavior in lieu of hair-pulling. This could involve making a fist or sitting on their hand. The final component is social support, whereby TTM patients are encouraged to involve their loved ones in hair-pulling accountability [38]. Two studies, one involving HRT alone and the other involving HRT plus acceptance and commitment therapy (ACT), demonstrated improvements in MGH-HPS and Yale-Brown Obsessive–Compulsive Scale

for Trichotillomania (Y-BCOS-TM) scores both immediately after and several months post-treatment in intervention groups [39,40]. One study explored the effectiveness of a “stepped care” model for treatment whereby subjects engaged in 10 weeks of behavior therapy, followed by eight weeks of HRT, compared to a waitlist control group. Upon study completion, the intervention group showed statistically significant improvements on the MGH-HPS, Psychiatric Institute Trichotillomania Scale (PITS), and quality of life measures [41]. Additionally, half of the subjects no longer met the diagnostic criteria for TTM, though this number decreased to 33% at the three-month follow-up [41]. Another study compared individuals receiving HRT alone to subjects receiving HRT after beginning an SSRI at least two months prior. While both groups showed improvements on MGH-HPS and Clinical Global Impressions Scale (CGI) after their respective interventions, the combination group demonstrated greater improvements [42]. A small, uncontrolled case series resulted in four of six participants reaching “near zero” pulling after a seven-week HRT intervention, with three subjects maintaining their progress at a three-month follow-up assessment [43]. Lastly, a 2021 study compared HRT to decoupling therapy. Though statistically significant improvements were observed on the Generic BFRB Scale (GBS) for both groups when comparing pre- and post-treatment values, the difference between groups was not significant [44].

4.3. Acceptance and Commitment Therapy (ACT)

ACT is a behavioral therapy technique whereby patients develop psychological flexibility by learning how to accept difficult emotions, thoughts, and urges without judgment. In doing this, individuals can begin to commit to making necessary or desired behavior changes and focus on their values and long-term goals instead of on their negative emotions [45]. One randomized controlled trial by Lee et al. compared ACT to a waitlist control group. After 10 sessions, the ACT group saw a 46.6% drop in MGH-HPS scores and a 77% drop in the self-reported number of hairs pulled per day compared to the waitlist, which saw 0% and 10% decreases in these measures, respectively [46]. Another small study of five individuals with TTM averaged an 88% reduction in pulling after eight sessions of combination ACT/HRT treatment [47]. However, at three-month follow-up, only two participants maintained their progress, with two losing half of their treatment gains and one individual regressing to pre-treatment severity [47]. In contrast, the combination ACT/HRT study by Woods and colleagues referenced in the HRT section demonstrated improvements in MGH-HPS and Y-BCOS-TM scores, both immediately after and several months post-treatment, in the intervention group as compared to the waitlist group [40].

4.4. Decoupling Therapy (DC)

DC is similar to HRT, except the replacement behavior mimics a pulling action, such as tugging at a piece of string or on one’s earlobe [48]. Two studies explored DC in comparison to progressive muscle relaxation (PMR) [48,49]. A study by Moritz and Rufer demonstrated that DC showed a significantly greater decrease in hair-pulling severity on the MGH-HPS compared to PMR [48]. A study by Weidt and colleagues found that while both the DC and PMR groups’ MGH-HPS scores improved, the DC group’s improvement was not significantly different from that of the PMR group. Interestingly, both groups maintained their progress six months after the intervention [49]. A third study conducted in 2021 compared DC with HRT. As discussed in the HRT section, both groups saw statistically significant improvements on the GBS, but the difference between groups was not statistically significant [44].

4.5. Dialectical Behavior Therapy (DBT)

DBT is a type of psychotherapy that teaches skills in emotion regulation, mindfulness, and distress tolerance [50]. Commonly used for the treatment of borderline personality disorder, DBT has only been explored for BFRBs in the last few decades [50]. One study of 10 subjects undergoing DBT for eleven weeks showed significant improvement in the

hair-pulling severity on the MGH-HPS, Trichotillomania Impairment Scale (TIS), and impairment measures of the CGI after intervention [51]. At three- and six-month follow-ups, five subjects were considered “full responders” and four were considered “partial responders”, noting the maintenance of improved scores on assessment scales [52]. Another study compared a DBT group to a minimal attention control (MAC) group, where DBT subjects received one session per week and MAC group participants received a weekly “check-in” phone call for 11 weeks. The DBT group showed significant improvements on the MGH-HSP, Trichotillomania Severity Scale (TSS), and TIS when compared to their own baseline scores and when compared to the MAC group upon treatment completion [53]. At three- and six-month follow-up assessments, MGH-HSP and TSS scores worsened, but the TIS scores were maintained or slightly improved [53].

4.6. Antipsychotics

Antipsychotic medications have numerous uses in psychiatry, including in the treatment of schizophrenia, acute mania, agitation, delusional disorder, or Tourette syndrome. These medications are categorized as either typical (first-generation) or atypical (second-generation). Typical antipsychotics antagonize the dopamine D2 receptor in the CNS, thereby reducing dopamine neurotransmission [54]. These medications also contain anticholinergic, anti-histaminergic, and anti-noradrenergic properties. Atypical antipsychotics similarly reduce dopamine neurotransmission but do so through partial agonism at D2 receptors with more rapid dissociation as compared to first-generation antipsychotics [54]. They additionally block the serotonin receptor, 5-HT_{2A} [54]. One proposed etiology of TTM is dysregulation within the dopamine-modulated basal ganglia, hence the theory that dopaminergic drugs could potentially help with TTM management [12]. Two studies exploring the typical antipsychotics Haloperidol and Pimozide enrolled subjects who were currently taking SSRIs but had not experienced notable improvement in their TTM symptoms. After the introduction of the antipsychotic to their medication regimen, 89% and 86% of participants were considered responders to Haldol and Pimozide, respectively [55,56]. One open-label Olanzapine study had 13 individuals take the atypical antipsychotic for three months. Upon trial completion, subjects averaged 66% improvement in MGH-HPS scores, including four subjects who achieved complete symptom remission. At a follow-up assessment one month later, 33% of subjects had experienced some degree of relapse [57]. A twelve-week, placebo-controlled Olanzapine study resulted in 85% of the treatment group and 17% of the placebo group being considered responders on the CGI scale, with significant improvements in Y-BOCS-TM scores as well [58]. Two small Risperidone studies explored atypical antipsychotics as augmentation therapy in patients refractory to either SSRIs or another antipsychotic. One study demonstrated varying degrees of improvement after four weeks of daily Risperidone in five subjects [59]. Three patients had significant clinical improvements, one with minimal improvement, and one with no changes in the Y-BOCS-TM [59]. Of the three responders, two maintained their progress for “some months”, but the follow-up timepoints were not specified by the authors. The final responder discontinued the medication after three months due to increased depressive symptoms with the medication. Another case series reported on three individuals who augmented either an SSRI or Perphenazine with Risperidone [60]. Two subjects taking Fluoxetine saw an average decrease of 54% and 38% in Y-BOCS and PITS scores, respectively, after adding Risperidone to their medication regimen [60]. The third individual, previously taking the first-generation antipsychotic Perphenazine, became pull-free after adding Risperidone. The last Risperidone study is a case report of an 85-year-old woman who achieved remission from new-onset TTM after starting a combination of low-dose Risperidone and Naltrexone [61]. The patient became symptom-free after two weeks and tapered her medications over the course of six months [61]. Finally, one uncontrolled study explored Aripiprazole in 11 subjects for an eight-week trial. Upon completion, 64% of subjects were considered responders to treatment on the CGI scale and averaged a 50% reduction in MGH-HPS scores [62].

4.7. Tricyclic Antidepressants (TCAs)

TCAs prevent the reuptake of serotonin and norepinephrine into neurons, causing these neurotransmitters to remain active [63]. Serotonin aids in mood and behavior regulation, while norepinephrine modulates emotions and aids in attention [63]. In addition to treating depression, TCAs are sometimes used for anxiety disorders and OCD, all of which frequently co-occur with TTM [64]. In a ten-week crossover study of Clomipramine and Desipramine in 13 subjects, Physician Rating Scale (PRS) scores improved by an average of 53% with Clomipramine, compared to 13% with Desipramine, which was statistically significant. Additionally, TIS scores were significantly improved by 38% with Clomipramine compared to 9% with Desipramine. Upon trial completion, 12 subjects continued Clomipramine treatment. At a six-month follow-up assessment, three subjects had achieved complete remission and nine had either improved or unchanged clinical scale scores, indicating that progress was maintained. [65]. One parallel-treatment study comparing Clomipramine with CBT and placebo groups found that Clomipramine was more effective than placebo when comparing post-treatment TSS, TIS, and CGI scores with pre-treatment values, but the differences fell short of statistical significance [32]. Furthermore, the CBT group showed statistically significant improvement compared to both Clomipramine and placebo groups. Lastly, in a case series of four subjects treated with Clomipramine, all experienced symptom reduction initially; however, at a three-month follow-up, 75% of subjects had relapsed to pre-treatment symptom severity despite continuing the same, previously effective dose of Clomipramine [66].

4.8. Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs prevent the reuptake of serotonin into neurons and are utilized for MDD, anxiety disorders, and OCD [33]. Since TTM is considered along the OCD spectrum and since many OCD sufferers have achieved symptom relief with SSRIs, it is plausible that TTM could stem from serotonergic dysfunction and experience symptom relief with SSRIs as well [33]. Several SSRIs have been explored, including Fluoxetine, Fluvoxamine, Citalopram, and Escitalopram. Of the six Fluoxetine studies, three reported no significant changes in hair-pulling severity compared to waitlist or placebo groups [33,67,68]. Two open-label Fluoxetine studies saw an average of 34–58% improvement in Y-BCOS-TM and PITS scores after completing two to four months of treatment [69,70]. In a retrospective chart review of six TTM patients taking Fluoxetine, 100% of patients experienced a reduction in symptoms, measured by the patient-reported number of hairs pulled per day, within four weeks of initiating treatment; however, five of the six patients experienced relapses to pre-treatment severity by week nine despite continuing the medication [71]. Fluvoxamine has been studied in two open-label trials [72,73]. One eight-week study by Christenson and colleagues demonstrated an average decrease (improvement) of 44% on PRS, as well as a 51% decrease in patient-reported hair-pulling episodes, which were both statistically significant, in a group of 14 subjects. Despite the group's modest improvements, only four subjects were considered responders on assessment scales [72]. Of these four, three continued Fluvoxamine after trial completion and had "substantially lost" clinical gains at a six-month follow-up assessment [72]. The second Fluvoxamine study by Stanley et al. saw improvement in some hair-pulling measures, such as duration and resistance, as well as improvements in depressive symptoms, but this study did not assess long-term efficacy with follow-up [73]. Citalopram was explored in one open-label study of 13 subjects. After 12 weeks of treatment, 39% of participants were considered responders to treatment on the CGI scale [74]. Lastly, one open-label trial by Gadde and colleagues explored Escitalopram in 16 subjects. By the end of this 12-week trial, eight subjects were considered responders with greater than 50% improvement on the TSS [75].

4.9. N-Acetylcysteine (NAC)

N-acetylcysteine, an amino acid derivative and regulator of glutamate release, has been studied as a potential treatment for TTM since the early 2000s. Glutamatergic dysfunction

is suspected to play a role in OCD, specifically, a mutation in the *SLC1A1* glutamate transporter gene [76]. Since TTM is classified as a disorder on the OCD spectrum, it is proposed that glutamate dysregulation could underlie the etiology of TTM as well [77]. Additionally, not only has the incorporation of NAC reduced excessive grooming and repetitive behaviors in animal models, but studies examining NAC as a treatment for other BFRBs, like skin picking and nail-biting, have also yielded promising results [78–80]. One double-blind, placebo-controlled study from 2009 used this supplement in 44 subjects. After nine weeks of treatment, 56% of the NAC group were considered responders to treatment, compared to 16% of the placebo group utilizing the CGI. Furthermore, the NAC group's MGH-HPS post-treatment scores had an average decrease of 41%, whereas the placebo group saw a 0% decrease [77]. The differences between groups for both outcome measures were statistically significant [77]. A case study of two individuals treated with NAC for three months reported that both subjects were considered responders on the CGI. Additionally, these individuals maintained their progress at a six-month follow-up assessment [80].

4.10. Inositol

Inositol is an integral component of the phosphatidyl inositol (IP3) second-messenger system in human cells. This intracellular system is associated with various neurotransmitters, including serotonin, dopamine, and glutamate receptors [81]. Prior studies investigating this supplement as a potential treatment for OCD have yielded encouraging results [82]. A study from 2017 explored treatment with Inositol in 31 people with TTM. After the ten-week trial, 42% of the inositol group and 50% of the placebo group were considered responders on the CGI, with no significant differences between groups [81]. Conversely, a case study of two subjects who took inositol for eight to 12 weeks reported that both individuals were considered responders on the CGI scale upon study completion [83].

4.11. Naltrexone

Naltrexone is an opioid antagonist that is FDA-approved to treat opioid and alcohol use disorders [84]. By blocking central and peripheral opioid mu receptors, this medication prevents the sedating and euphoric effects of these substances, thereby discouraging their use [84]. One typical component of TTM is experiencing a sense of relief or pleasure once a hair is pulled. Thus, it is hypothesized that Naltrexone could potentially lessen this sense of pleasure gained from hair-pulling and disrupt the activated reward pathways in the brain. A study by Grant et al. recruited 51 subjects with TTM to receive either Naltrexone or a placebo for eight weeks. Upon study completion, MGH-HPS scores improved by 25% in the Naltrexone group and by 27% in the placebo group, with no significant differences between groups [85]. TSS scores improved by 34% and 32% in the Naltrexone and placebo groups, respectively, and only 9% of subjects in each group were considered responders to treatment on the CGI. These differences were also not statistically significant [85]. This is the only clinical trial investigating Naltrexone for TTM in adults to date; however, a case of successful remission with Naltrexone and Risperidone is also present in the literature. A case report from Slovenia describes new-onset TTM in an 85-year-old woman. This patient achieved remission of symptoms after two weeks on a combination of low-dose Risperidone and Naltrexone [61].

4.12. Dronabinol

A cannabinoid agonist, Dronabinol, serves as synthetic tetrahydrocannabinol (THC), and is currently FDA-approved for the treatment of chemotherapy-induced nausea, vomiting, and anorexia [86]. Cannabinoid CB1 receptors are highly expressed in the basal ganglia, an area of the brain responsible for motor regulation, lending support to the hypothesis that disruption of signaling within the endocannabinoid system could contribute to developing body-focused repetitive behaviors like TTM [87]. The first study to explore Dronabinol as a potential treatment comprised 12 subjects who received Dronabinol daily for 12 weeks.

As a group, subjects achieved statistically significant improvements in MGH-HPS scores, and nearly two-thirds of subjects were considered responders on the CGI scale upon study completion [88]. In contrast, a double-blind, placebo-controlled study conducted nearly a decade later failed to demonstrate a statistically significant improvement in subjects who took Dronabinol compared to the placebo group during a 10-week trial [89].

A comprehensive summary of each study referenced in these sub-sections can be found below in Table 1.

Table 1. Summary of studies on trichotillomania treatment, including intervention, study design, number of subjects per group, duration of treatment, follow-up assessment timepoints, assessment scales utilized, and study outcomes.

First Author, Year	Intervention	Study Design	Treatment Group	Control or Placebo Group(s)	Study Duration	Follow-Up	Clinical Scales or Assessments Used	Intervention Outcomes
Ninan, 2000 [32]	CBT	RCT: parallel design	<i>n</i> = 6	Clomipramine <i>n</i> = 5; placebo <i>n</i> = 6	9 weeks	None	NIMH-TSS, NIMH-TIS, CGI	CBT significantly more effective than Clomipramine and placebo groups.
van Minnen, 2003 [33]	CBT	RCT: parallel design	<i>n</i> = 14	Fluoxetine <i>n</i> = 11; waitlist <i>n</i> = 15	12 weeks	None	MGH-HPS	CBT superior to Fluoxetine and waitlist groups.
Toledo, 2015 [34]	CBT	RCT: parallel design	<i>n</i> = 22	Supportive therapy <i>n</i> = 22	22 weeks	None	MGH-HPS, CGI	Significant improvement with CBT compared to supportive therapy.
Keijsers, 2016 [35]	CBT	RCT: parallel design	<i>n</i> = 26	Behavior therapy <i>n</i> = 22	12 weeks	3, 12, 24 months	MGH-HPS, SURF	No significant difference in improvement between groups.
Mass, 2018 [36]	CBT	RCT: parallel design	<i>n</i> = 27	Cognitive bias training and CBT <i>n</i> = 27	18 weeks	1, 3, 12 months	MGH-HPS, SURF	No significant differences in improvement between groups. Significant relapse in both groups by 12 month follow-up.
Slikboer, 2020 [37]	CBT	Uncontrolled, longitudinal	<i>n</i> = 6	None	3 days	6, 12 months	MGH-HPS	All subjects had varying levels of responsiveness and relapse rates.
Shareh, 2017 [39]	HRT	RCT: parallel design	<i>n</i> = 22	Waitlist <i>n</i> = 17	8 weeks	1, 6, 12 months	MGH-HPS, Y-BOCS-TM	Significant improvement with HRT compared to waitlist group.
Rogers, 2014 [41]	BT, then HRT	RCT: parallel design	<i>n</i> = 41	BT alone <i>n</i> = 19; waitlist <i>n</i> = 30	18 weeks	3 months	MGH-HPS, PITS	Significant improvement with BT and HRT compared to BT and waitlist groups.
Dougherty, 2006 [42]	HRT	RCT: parallel design	<i>n</i> = 6	HRT and Sertraline <i>n</i> = 11	22 weeks	None	MGH-HPS, CGI	HRT and Sertraline superior to HRT alone.
Twohig, 2004 [43]	HRT	Case series	<i>n</i> = 6	None	7 weeks	3 months	MGH-HPS	A total of 67% considered responders to treatment. Of responders, 75% maintained progress at follow-up.
Moritz, 2021 [44]	HRT	RCT: parallel design	<i>n</i> = 17	DC therapy <i>n</i> = 27	4 weeks	None	GBS	Both groups with statistically significant improvements, but no significant difference between groups.
Woods, 2006 [40]	HRT + ACT	RCT: parallel design	<i>n</i> = 12	Waitlist <i>n</i> = 13	12 weeks	3 months	MGH-HPS, NIMH-TIS	Significant improvement with ACT and HRT compared to waitlist group.
Crosby, 2012 [47]	HRT + ACT	Open clinical trial	<i>n</i> = 5	None	8 weeks	3 months	MGH-HPS, daily self-tracking	All responded to treatment; 40% maintained progress at follow-up.

Table 1. Cont.

First Author, Year	Intervention	Study Design	Treatment Group	Control or Placebo Group(s)	Study Duration	Follow-Up	Clinical Scales or Assessments Used	Intervention Outcomes
Lee, 2018 [46]	ACT	RCT: parallel design	<i>n</i> = 12	Waitlist <i>n</i> = 13	10 weeks	3 months	MGH-HPS, daily self-tracking	Significant improvement with ACT compared to waitlist group.
Moritz, 2011 [48]	DC	RCT: parallel design	<i>n</i> = 20	PMR <i>n</i> = 20	4 weeks	None	MGH-HPS	Significant improvement with DC compared to PMR.
Weidt, 2015 [49]	DC	RCT: parallel design	<i>n</i> = 55	PMR <i>n</i> = 50	4 weeks	6 months	MGH-HPS	No statistically significant difference between DC and PMR groups.
* Moritz, 2021 [44]	DC	RCT: parallel design	<i>n</i> = 27	HRT <i>n</i> = 17	4 weeks	None	GBS	No statistically significant difference between DC and HRT groups.
Keuthen, 2010 [51,52]	DBT	Open clinical trial	<i>n</i> = 10	None	11 weeks	3, 6 months	PITS, MGH-HPS, CGI, NIMH-TIS	A total of 82% considered either partial or full responders.
Keuthen, 2012 [53]	DBT	RCT: parallel design	<i>n</i> = 20	MAC <i>n</i> = 18	11 weeks	3, 6 months	PITS, MGH-HPS, NIMH-TSS and TIS, CGI	Significant improvement with DBT compared to MAC group.
* van Minnen, 2003 [33]	SSRI, Fluoxetine	RCT: parallel design	<i>n</i> = 11	Behavior therapy <i>n</i> = 14; waitlist <i>n</i> = 15	12 weeks	None	MGH-HPS	No statistically significant difference between Fluoxetine and waitlist groups. Behavior therapy superior to both.
Christenson, 1991 [67]	SSRI, Fluoxetine	RCT: crossover	<i>n</i> = 15	Placebo <i>n</i> = 15	6 weeks per treatment, 5 week washout	None	Various patient-reported measures	No significant difference between groups.
Streichenwein, 1995 [68]	SSRI, Fluoxetine	RCT: crossover	<i>n</i> = 16	Placebo <i>n</i> = 16	12 weeks per treatment, 5 week washout	None	Physical exam, patient-reported severity and number of hairs pulled	No significant difference between groups.
Koran, 1992 [69]	SSRI, Fluoxetine	Open-label	<i>n</i> = 13	None	8–12 weeks	None	Y-BOCS-TM	A total of 53% considered responders.
Winchel, 1992 [70]	SSRI, Fluoxetine	Open-label	<i>n</i> = 12	None	16 weeks	None	MGH-HPS, PITS	A total of 67% considered responders.
Iancu, 1996 [71]	SSRI, Fluoxetine	Open-label	<i>n</i> = 6	None	6–20 weeks	None	Patient-reported quantity and frequency of hairs pulled	A total of 17% considered responders.
Stanley, 1997 [73]	SSRI, Fluvoxamine	Open-label	<i>n</i> = 13	None	12 weeks	None	Y-BOCS-TM	Significant improvements in some severity measures. Significant improvement in compulsion and resistance measures.

Table 1. Cont.

First Author, Year	Intervention	Study Design	Treatment Group	Control or Placebo Group(s)	Study Duration	Follow-Up	Clinical Scales or Assessments Used	Intervention Outcomes
Christenson, 1998 [72]	SSRI, Fluvoxamine	Open-label	$n = 14$	None	8 weeks	6 months	NIMH-TSS, NIMH-TIS, NIMH-PRS, patient-reported hair-pulling episodes	A total of 29% considered responders. Regression towards baseline scores at follow-up.
Stein, 1997 [74]	SSRI, Citalopram	Open-label	$n = 13$	None	12 weeks	None	Y-BOCS-TM, CGI, NIMH	A total of 39% considered responders.
Gadde, 2007 [75]	SSRI, Escitalopram	Open-label	$n = 16$	None	12 weeks	None	CGI, NIMH-TSS	A total of 50% considered responders.
Van Ameringen, 1999 [55]	Antipsychotic, Haloperidol alone or with an SSRI	Open-label	$n = 9$	None	Not specified	None	Patient-reported hair-pulling episodes, pulling site depilation severity	A total of 89% considered responders.
Stein, 1992 [56]	Antipsychotic, Pimozide + SSRI	Open-label	$n = 7$	None	Not specified	None	CGI	A total of 86% considered responders.
Stewart, 2003 [57]	Antipsychotic, Olanzapine	Open-label	$n = 13$	None	12 weeks	1 month	MGH-HPS, CGI	All subjects responded; 33% had relapsed at follow-up.
Van Ameringen, 2010 [58]	Antipsychotic, Olanzapine	RCT: parallel design	$n = 13$	Placebo $n = 12$	12 weeks	12 months	Y-BOCS-TM, CGI	Significant improvement with Olanzapine compared to placebo group.
Epperson, 1999 [60]	Antipsychotic, Risperidone + SSRI or Perphenazine	Case series	$n = 3$	None	6–30 weeks	None–8 months	Y-BOCS-TM, PITS	All subjects responded, with varying levels of symptom improvement.
Stein, 1997 [59]	Antipsychotic, Risperidone + SSRI	Open-label	$n = 5$	None	4 weeks	None	Y-BOCS-TM, CGI	A total of 60% considered responders.
Oravec, 2014 [61]	Risperidone + Naltrexone	Case study	$n = 1$	None	2 weeks	None	None	Subject responded after two weeks of treatment.
White, 2011 [62]	Antipsychotic, Aripiprazole	Open-label	$n = 11$	None	8 weeks	None	MGH-HPS, CGI	A total of 64% considered responders.
Swedo, 1989 [65]	TCA, Clomipramine and Desipramine	RCT: crossover	$n = 13$	None	10 weeks, no washout	4, 6 months	NIMH-TIS, NIMH-TSS, NIMH-PRS	Clomipramine statistically superior to Desipramine.
* Ninan 2000 [32]	TCA, Clomipramine	RCT: parallel design	$n = 5$	CBT $n = 6$; placebo $n = 6$	9 weeks	None	NIMH-TSS, NIMH-TIS, CGI-I	No statistically significant difference between Clomipramine and placebo groups. CBT significantly superior to both.
Pollard, 1991 [66]	TCA, Clomipramine	Case series	$n = 4$	None	Not specified	3 months	Unspecified	All subjects responded, but 75% relapsed at follow-up.
Grant, 2009 [77]	NAC	RCT: parallel design	$n = 22$	Placebo $n = 22$	12 weeks	None	MGH-HPS, CGI, PITS	Significant improvement with NAC compared to placebo.

Table 1. Cont.

First Author, Year	Intervention	Study Design	Treatment Group	Control or Placebo Group(s)	Study Duration	Follow-Up	Clinical Scales or Assessments Used	Intervention Outcomes
Rodrigues-Barata, 2012 [80]	NAC	Case series	<i>n</i> = 2	None	3 months	6 months	Physician assessment of hair growth	Both subjects responded to treatment.
Leppink, 2017 [81]	Inositol	RCT: parallel design	<i>n</i> = 19	Placebo <i>n</i> = 12	10 weeks	None	MGH-HPS, NIMH-TSS, CGI	No significant difference between groups
Seedat, 2001 [83]	Inositol	Case series	<i>n</i> = 2	None	8–12 weeks	None	CGI	Both subjects responded to treatment.
Grant, 2014 [85]	Naltrexone	RCT: parallel design	<i>n</i> = 20	Placebo <i>n</i> = 24	8 weeks	None	MGH-HPS, NIMH-TSS	No significant difference between groups.
Grant, 2011 [88]	Dronabinol	Open-label	<i>n</i> = 12	None	12 weeks	None	MGH-HPS, CGI	A total of 67% considered responders.
Grant, 2022 [89]	Dronabinol	RCT: parallel design	<i>n</i> = 34	Placebo <i>n</i> = 16	10 weeks	None	NIMH-TSS, CGI	No significant difference between groups.

* Indicates that the study has been previously listed in the table, but emphasizes a different treatment modality. Abbreviations: CBT, cognitive behavioral therapy; BT, behavior therapy; HRT, habit reversal training; ACT, acceptance and commitment therapy; DC, decoupling therapy; DBT, dialectical behavior therapy; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants; NAC, N-acetylcysteine; RCT, randomized controlled trial; MAC, minimal-attention control; PMR, progressive muscle relaxation; MGH-HPS, Massachusetts General Hospital Hair-Pulling Scale; NIMH-TSS, Trichotillomania Severity Scale; NIMH-TIS, Trichotillomania Impairment Scale; NIMH-PRS, Physician Rating Scale; CGI-I, Clinical Global Impressions Severity and Improvement Scale; GBS, Generic Body-Focused Repetitive Behavior Scale; Y-BOCS-TM, Yale-Brown Obsessive-Compulsive Scale-Trichotillomania; PITS, The Psychiatric Institute Trichotillomania Scale.

5. Discussion

Trichotillomania is a challenging disorder to treat. Despite sharing features and co-occurring with several psychiatric disorders, its etiology remains unclear, potentially stemming from a combination of neurochemical, genetic, or environmental causes. When comparing treatments established in the literature, behavioral interventions appear to be the most reliable for achieving symptom relief. This aligns with the current treatment guidelines, which advise clinicians to incorporate some form of behavioral therapy into their treatment regimen, with CBT and HRT most commonly recommended [1,38]. Based on the CBT and HRT studies, CBT appears effective in the short term, while HRT data suggest that improvements in hair-pulling severity may have better longevity given the continual progress demonstrated at various follow-up points in HRT studies. Thus, if clinicians decide to use CBT, study results suggest this technique may need to be implemented at regular intervals throughout a patient's life to maintain progress. DC therapy also appears effective, with a significant reduction in hair-pulling noted after the intervention when compared to pre-intervention baseline measures both immediately after completion and at follow-up points [48,49]. The 2021 study comparing DC to HRT showed improvement with both treatments, but since the difference between groups was not statistically significant, it is unclear if one is superior [44]. Lastly, while DBT and ACT studies demonstrated short-term improvement in severity and impairment measures, less than half of subjects between these studies maintained their progress long-term [47,52,53]. However, it should be noted that the two DBT studies and one ACT study incorporated CBT or HRT in addition to these modalities, rather than DBT or ACT alone. This significant caveat, along with the small sample sizes of the individual studies, suggests that DBT and ACT need more exploration before it can be determined if either of these techniques could serve as reliable treatments.

Regarding the pharmacological treatment options, the results of NAC studies are encouraging, with subjects who received the intervention demonstrating notable reductions in hair-pulling severity in both the placebo-controlled trial and two case studies [77,80]. The results from the inositol studies are inconclusive, with the randomized controlled trial failing to demonstrate significant differences in study outcomes between groups, while the case studies did demonstrate a response to treatment [81,83]. Dronabinol's efficacy remains ambiguous, as the open-label trial saw the majority of participants respond to treatment, while the randomized controlled trial did not yield significant differences between the Dronabinol and placebo groups [88,89]. Larger, placebo-controlled studies with regular follow-up assessments are needed for NAC, Inositol, and Dronabinol to establish their efficacy as potential treatments. Given the mild side effect profiles and few drug–drug interactions of both NAC and Inositol, there is minimal risk if providers wish to trial one or both supplements in their TTM patients [90,91]. Despite that the combination of Naltrexone and Risperidone demonstrated rapid symptom remission in the geriatric patient case discussed, the randomized controlled trial of Naltrexone failed to demonstrate differences in hair-pulling severity between the experimental and placebo groups; thus, using this medication to treat TTM is not well-supported by the literature at this time [61,77]. However, since Naltrexone is approved for opioid and alcohol use disorders, this medication could be trialed in TTM patients with these co-occurring addictions [84]. Regarding TCAs, while the crossover study demonstrated Clomipramine as superior to Desipramine, the placebo-controlled Clomipramine study failed to demonstrate significant differences between these two groups [32,65]. While the Clomipramine case series showed notable improvements upon initiation of treatment, most subjects' symptoms regressed to pre-treatment baseline severity at a three-month follow-up assessment despite continuing the medication [66]. With the advent of SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs), TCAs are now less frequently utilized in psychiatry, typically reserved for MDD refractory to first- and second-line therapies [63]. One notable reason for this shift is due to the anticholinergic and antihistamine side effect profiles, narrow therapeutic index, low threshold for overdose, and potentially deleterious drug–drug interactions with other psychotropic medications [63]. Given the high psychiatric co-morbidity that occurs

with TTM, patients and study subjects may already take other psychoactive medications like SSRIs, which are not recommended to combine with TCAs, making studying this medication class logistically difficult [63]. The results of the antipsychotic studies appear encouraging; however, there are several notable limitations. In addition to needing larger study populations, all but one study was uncontrolled, limiting researchers' ability to rule out placebo effects [55–57,59–62]. Second, while most subjects enrolled in the Haloperidol, Pimozide, and Risperidone trials demonstrated significant reduction in hair-pulling symptoms, these medications were administered as augmentation to SSRIs or Perphenazine in subjects who had not seen improvement with those medications alone [55,56,59–61]. While it is reasonable to deduce that the documented improvements were, at least in part, due to the addition of the antipsychotic, synergistic or placebo effects cannot be excluded. The open-label Olanzapine and Aripiprazole studies render similar concerns given their design and small sample sizes [57,62]. Lastly, SSRIs are the most studied interventions for TTM to date. Of the six Fluoxetine studies, three were uncontrolled, and none of the randomized controlled trials demonstrated significant improvements when the drug was compared to a placebo or another intervention [33,67,68]. The other SSRI studies showed significant decreases in hair-pulling severity in 50% or less of experimental group subjects [72–75]. One notable exception is the HRT study by Dougherty and colleagues, in which HRT plus Sertraline (an SSRI) was used as a comparison group to those receiving HRT alone. The combination group demonstrated statistically significant improvement in severity and impairment measures compared to the HRT group [42]. Despite inconclusive data from the clinical trials discussed, SSRIs remain the most prescribed medication for TTM [2]. One potential explanation for this discrepancy could be the relatively mild side effect profile of SSRIs compared to antipsychotics and TCAs [54,63]. Another potential explanation is that SSRIs may help with the anxious or depressive symptoms that occur because of TTM, even though they may not address the root of the disorder itself. This assertion is supported by the fact that while many patients in SSRI clinical trials saw regression to pre-treatment severity during or after treatment, improvements in secondary outcomes like anxiety, depression, or life impairment were often maintained at follow-up timepoints [65,71,72,76]. While the effectiveness of SSRIs as monotherapy for TTM is not reliably demonstrated in the literature, evidence from the HRT, Pimozide, Haloperidol, and Risperidone studies noted that reductions in hair-pulling improved when these medications were combined with an SSRI, providing some evidence that SSRIs may be more effective as combination therapy rather than monotherapy for this disorder [42,55,56,59–61].

6. Limitations

The authors acknowledge several limitations of this literature review. First, a limited number of databases were utilized to find the discussed studies, so it is certainly possible that not all studies conducted per treatment modality were found. Next, no study had a sizable enough population to make results generalizable, as the largest study totaled 50 participants between experimental and control groups [89]. In addition to small sample sizes, there is a tremendous lack of randomized controlled trials pertaining to pharmacological interventions. Of the 28 pharmacological studies discussed, only 9 were randomized controlled trials. Thus, the majority of data regarding pharmacological interventions in adult TTM come from open-label studies, case series, and case reports, leading clinicians to have to interpret results from these studies with an abundance of caution. Another limitation is the accessibility of the treatment options discussed in this review, as not all treatment options are equally available across the globe. For example, while N-acetylcysteine is widely available as an over-the-counter dietary supplement in the United States, Canada, and Australia, patients in many other countries can only obtain this substance through a prescription [90]. Furthermore, even if all the discussed treatments are available where one lives, not all treatments are suitable for every patient, which is why it is imperative for clinicians to evaluate for and take into consideration co-occurring psychological disorders [1]. For example, a clinician wishing to trial Olanzapine in their patient with TTM should

ensure this patient is not being treated for ADHD with a stimulant, as these medications have opposing effects on dopamine [54]. Similarly, a patient being treated with an SSRI for major depressive disorder should not be prescribed TCA for TTM, as this drug combination increases the risk for serotonin syndrome [54]. Finally, another limitation of the studies is the lack of follow-up on treatment, as less than half of them involved some form of follow-up assessment. Assessing long-term treatment efficacy is imperative, as this impacts the chronicity of treatment and helps manage patient expectations.

7. Conclusions and Recommendations

Trichotillomania is a complex psychological disorder that is relatively common but marginally understood. There is evidence to suggest that the disorder's etiology could be composed of genetic, neurobiological, and environmental factors. Current clinical guidelines overwhelmingly recommend behavioral therapy, specifically, HRT, which is supported by the literature. Of the data presented, study results also suggest that patients could benefit greatly from CBT, so long as clinicians implement regular maintenance sessions to avoid relapse. Though recent research into different pharmacological agents is encouraging, a review of the studied interventions does not render clear treatment guidance. Numerous limitations, such as small sample sizes, a lack of randomized controlled trials, and sparse follow-up assessments, make the results of many studies difficult to interpret. Current treatment recommendations do not seem to favor any pharmacological option over another. Based on our paper, if pharmacological therapy is to be used for adult TTM, it may be more effective in combination with a behavioral strategy, as supported by some studies. Though the results of SSRI studies are inconclusive, these medications may still be beneficial in addressing the anxious and depressive symptoms that often co-occur with TTM. Lastly, though the supplements NAC and Inositol have not been as extensively studied compared to some of the other medications discussed, the mild side effect profiles make trialing these supplements for TTM treatment a low-risk and potentially beneficial endeavor.

Based on the results of the trials discussed, it is evident that additional double-blind, placebo-controlled studies are still necessary to determine what a reliable treatment for TTM looks like. In particular, randomized controlled trials of N-acetylcysteine, Inositol, Naltrexone, and Dronabinol merit replication, as only one double-blind, placebo-controlled study has been conducted for each of these interventions. Randomized controlled trials of antipsychotics are also warranted since all but one study examining these medications was open-label. We would prioritize researching second-generation antipsychotics like Olanzapine or Risperidone due to their milder side-effect profiles compared to first-generation antipsychotics. Additionally, studies comparing monotherapy with combination therapy (ex: CBT alone compared to CBT plus an SSRI) would be beneficial to evaluate if a more robust treatment response can be achieved with combination therapy. Regardless of what treatment approach is evaluated, the study design should include follow-up assessments to assess the longevity of the investigated intervention. Though this review emphasizes treatment interventions, it is also imperative to conduct studies dedicated to uncovering the etiology of TTM, as understanding the etiology will lend better treatment guidance for the disorder. Though the amount of research still needed is daunting, we are encouraged by the work conducted thus far by the small but dedicated group of researchers committed to finding solutions for this under-represented patient population.

Author Contributions: Conceptualization, L.P.B.; methodology, L.P.B.; data curation, L.P.B.; writing—original draft preparation, L.P.B. and R.R.; writing—review and editing, L.P.B. and R.R.; visualization, L.P.B. and R.R.; supervision, R.R. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding. The APC was funded by Rocky Vista University College of Osteopathic Medicine.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

Appendix A

Table A1. Clinical scales used as primary outcomes to assess trichotillomania symptom severity, psychological impairment, and treatment progress.

Clinical Scale	Description
Massachusetts General Hospital Hair-Pulling Scale (MGH-HPS)	The MGH-HPS is a 7-question, patient-rated assessment that utilizes a Likert scale to assess pulling severity and resistance/control abilities. Each question is scored from 0 to 4, with total scores ranging from 0 to 28. Higher scores reflect greater severity. This scale is particularly useful in documenting symptom change throughout treatment [81].
NIMH-Trichotillomania Severity Scale (NIMH-TSS) and NIMH-Trichotillomania-Impairment Scale (NIMH-TIS)	The TSS is a 5-question, clinician-rated assessment asking about time spent pulling within the past week and day, ability to resist urges to pull, functional impairment, and level of associated distress. Total scores ranging from 0 to 25. Higher scores reflect greater symptom severity. The TIS is a 1-item, clinician-rated assessment, meant to provide a “snapshot” of the patient’s clinical presentation and severity. Scores range from 0 to 10, with higher scores reflecting greater severity [64].
NIMH-Trichotillomania Physician Rating Scale (PRS)	The PRS is used to assess the severity of a patient’s trichotillomania symptoms. The baseline score is 10, with follow-up scores ranging from 0 to 20, with 0 indicating the absence of symptoms and 20 indicating “total incapacitation”, where virtually all waking hours are spent pulling [65].
Clinical Global Impressions Severity and Improvement Scale (CGI)	The CGI is a clinician-rated assessment meant to gauge a patient’s global functioning prior to and after treatment administration, especially drug treatments. These scales measure current symptom severity and the level of improvement since the last assessment, with scores ranging from 1 (very much improved) to 7 (very much worse). The CGI is not specific for trichotillomania, as it has been used for a wide array of psychiatric disorders [81].
Generic Body-Focused Repetitive Behavior Scale (GBS)	The GBS is an 8-item, patient-rated diagnostic scale devised in 2021. It was adapted from the Skin-Picking Scale-Revised (SPS-R) and Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) in order to evaluate any body-focused repetitive behavior. Questions pertain to symptom severity and life impairment over the past week [92].
Yale-Brown Obsessive–Compulsive Scale- Trichotillomania (Y-BOCS-TM)	Derived and adapted from the 67-question Yale-Brown Obsessive–Compulsive Scale (Y-BOCS), the Y-BOCS-TM is a 10-question, clinician-rated assessment measuring hair-pulling severity, specifically, intrusive thoughts and actual pulling behavior. Each question is scored from 0 to 5, with total scores ranging from 0 to 50. Higher scores indicate greater severity [64].
The Psychiatric Institute Trichotillomania Scale (PITS)	The PITS rates trichotillomania severity and can be used for baseline and progress assessment over time. The PITS scores six items related to TTM: number of body sites, severity of hair loss, time spent pulling, resistance to pulling urges, severity of feelings regarding pulling, and interference with daily functioning. Total scores range from 0 to 42 [93].
Severity Urge Resistance Frequency Scale (SURF)	The SURF is a collection of four, one-item questions that assess TTM symptom severity by quantifying hair-pulling urge and ability to resist the urge [35].

References

- Grant, J.E.; Chamberlain, S.R. Trichotillomania. *Am. J. Psychiatry* **2016**, *173*, 868–874. [CrossRef]
- França, K.; Kumar, A.; Castillo, D.; Jafferany, M.; Hyczy da Costa Neto, M.; Damevska, K.; Lotti, T. Trichotillomania (hair pulling disorder): Clinical characteristics, psychosocial aspects, treatment approaches, and ethical considerations. *Dermatol. Ther.* **2018**, *32*, e12622. [CrossRef]
- Mayo Clinic. Trichotillomania (Hair-Pulling Disorder)—Symptoms and Causes. Available online: <https://www.mayoclinic.org/diseases-conditions/trichotillomania/symptoms-causes/syc-20355188> (accessed on 5 April 2022).
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; American Psychiatric Publishing: Arlington, VA, USA, 2013.
- Grant, J.E.; Dougherty, D.D.; Chamberlain, S.R. Prevalence, gender correlates, and co-morbidity or trichotillomania. *Psychiatry Res.* **2020**, *288*, 112948. [CrossRef]

6. Christenson, G.A.; Mackenzie, T.B.; Mitchell, J.E. Characteristics of 60 adult chronic hair pullers. *Am. J. Psychiatry* **1991**, *148*, 365–370. [CrossRef]
7. Grant, J.E.; Redden, S.A.; Medeiros, G.C.; Tavares, H.; Odlaug, B.L.; Curley, E.E.; Keuthen, N.J. Trichotillomania and its clinical relationship to depression and anxiety. *Int. J. Psychiatry Clin. Pract.* **2017**, *21*, 302–306. [CrossRef]
8. Gershuny, B.S.; Keuthen, N.J.; Gentes, E.L.; Russo, A.R.; Emmott, E.C.; Jameson, M.; Dougherty, D.D.; Loh, R.; Jenike, M.A. Current posttraumatic stress disorder and history of trauma in trichotillomania. *J. Clin. Psychol.* **2006**, *62*, 1521–1529. [CrossRef]
9. Chesivoir, E.K.; Valle, S.; Grant, J.E. Comorbid trichotillomania and attention-deficit hyperactivity disorder in adults. *Compr. Psychiatry* **2022**, *116*, 152317. [CrossRef]
10. Keuthen, N.J.; Curley, E.E.; Scharf, J.M.; Woods, D.W.; Lochner, C.; Stein, D.J.; Tung, E.S.; Greenberg, E.; Stewart, S.E.; Redden, S.A.; et al. Predictors of comorbid obsessive-compulsive disorder and skin-picking disorder in trichotillomania. *Ann. Clin. Psychiatry* **2016**, *28*, 280–288.
11. Mamidi, P.; Gupta, K. Trichotillomania—An ayurvedic perspective. *AYUHOME* **2022**, *9*, 61–66. [CrossRef]
12. Hemmings, S.; Kinnear, C.; Lochner, C.; Seedat, S.; Corfield, V.; Moolman-Smook, J.; Stein, D. Genetic correlates in trichotillomania—A case-control association study in the south african caucasian population. *Isr. J. Psychiatry Relat. Sci.* **2006**, *43*, 93–101. Available online: https://doctorsonly.co.il/wp-content/uploads/2011/12/2006_2_5.pdf (accessed on 12 April 2022).
13. Zhang, G.; Stackman, R.W., Jr. The role of serotonin 5-HT_{2A} receptors in memory and cognition. *Front. Pharmacol.* **2015**, *6*, 255. [CrossRef]
14. De Deurwaerdere, P.; Chagraoui, A.; Di Giovanni, G. (Eds.) Multiple facets of serotonin modulation. In *5-HT Interaction with Other Neurotransmitters: Experimental Evidence and Therapeutic Relevance—Part B*; Elsevier Inc.: Amsterdam, The Netherlands, 2021; pp. 3–39, ISBN 978-0-444-64258-5.
15. Yokoyama, J.S.; Bonham, L.W.; Sturm, V.E.; Adhimoolum, B.; Karydas, A.; Coppola, G.; Miller, B.L.; Rankin, K.P. The 5-HTTLPR variant in the serotonin transporter gene modifies degeneration of brain regions important for emotion in behavioral variant frontotemporal dementia. *NeuroImage Clin.* **2015**, *9*, 283–290. [CrossRef]
16. Bocchio, M.; Fucsina, G.; Oikonomidis, L.; McHugh, S.B.; Bannerman, D.M.; Sharp, T.; Capogna, M. Increased serotonin transporter expression reduces fear and recruitment of parvalbumin interneurons of the amygdala. *Neuropsychopharmacology* **2015**, *40*, 3015–3026. [CrossRef]
17. Molloy, A.G.; Waddington, J.L. Assessment of grooming and other behavioural responses to the D1 dopamine receptor agonist SK & F 38393 and its R- and S-enantiomers in the intact adult rat. *Psychopharmacology* **1987**, *92*, 164–168. [CrossRef]
18. Wachtel, S.R.; Brooderson, R.J.; White, F.J. Parametric and pharmacological analyses of the enhanced grooming response elicited by the D1 dopamine receptor agonist SKF 38393 in the rat. *Psychopharmacology* **1992**, *109*, 41–48. [CrossRef]
19. Bienvenu, O.J.; Wang, Y.; Shugart, Y.Y.; Welch, J.M.; Grados, M.A.; Fyer, A.J.; Rauch, S.L.; McCracken, J.T.; Rasmussen, S.A.; Murphy, D.L.; et al. Sapap3 and pathological grooming in humans: Results from the OCD collaborative genetics study. *Am. J. Med. Genet. B Neuropsychiatr. Genet.* **2009**, *150B*, 710–720. [CrossRef]
20. O’Sullivan, R.L.; Rauch, S.L.; Breiter, H.C.; Grachev, I.D.; Baer, L.; Kennedy, D.N.; Keuthen, N.J.; Savage, C.R.; Manzo, P.A.; Caviness, V.S.; et al. Reduced basal ganglia volumes in trichotillomania measured via morphometric magnetic resonance imaging. *Biol. Psychiatry* **1997**, *42*, 39–45. [CrossRef]
21. Ghandili, M.; Munakomi, S. Neuroanatomy, Putamen. In *StatPearls*; StatPearls: Tampa, FL, USA, 2023. Available online: <https://www.ncbi.nlm.nih.gov/books/NBK542170/#:~:text=The%20putamen%20is%20involved%20in,%20cognitive%20functioning,%20and%20addiction> (accessed on 3 February 2023).
22. Knierim, J. *Neuroscience Online: An Electronic Textbook for the Neurosciences*. Department of Neurobiology and Anatomy; The University of Texas Medical School at Houston: Houston, TX, USA, 2020; Chapter 5, Section 3: Cerebellum.
23. Keuthen, N.J.; Makris, N.; Schlerf, J.E.; Martis, B.; Savage, C.R.; McMullin, K.; Seidman, L.J.; Schmahmann, J.D.; Kennedy, D.N.; Hodge, S.M.; et al. Evidence for reduced cerebellar volumes in trichotillomania. *Biol. Psychiatry* **2007**, *61*, 374–381. [CrossRef]
24. Stein, D.J. Functional brain imaging and pharmacotherapy in trichotillomania Single photon emission computed tomography before and after treatment with the selective serotonin reuptake inhibitor citalopram. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* **2002**, *26*, 885–890. [CrossRef]
25. Chamberlain, S.R.; Hampshire, A.; Menzies, L.A.; Garyfallidis, E.; Grant, J.E.; Odlaug, B.L.; Craig, K.; Fineberg, N.; Sahakian, B.J. Reduced brain white matter integrity in trichotillomania. *Arch. Gen. Psychiatry* **2010**, *67*, 965. [CrossRef]
26. Chamberlain, S.R.; Fineberg, N.A.; Blackwell, A.D.; Robbins, T.W.; Sahakian, B.J. Motor inhibition and cognitive flexibility in obsessive-compulsive disorder and trichotillomania. *Am. J. Psychiatry* **2006**, *163*, 1282–1284. [CrossRef]
27. Flessner, C.A.; Francazio, S.; Murphy, Y.E.; Brennan, E. An examination of executive functioning in young adult exhibiting body-focused repetitive behaviors. *J. Nerv. Men. Dis.* **2015**, *203*, 555–558. [CrossRef]
28. Christenson, G.A.; Mansueto, C.S. *Trichotillomania: Descriptive Characteristics and Phenomenology*; American Psychiatric Press, Inc.: Washington, DC, USA, 1999; pp. 1–41, ISBN 0-88048-759-3.
29. Boughn, S.; Holdom, J.J. The relationship of violence and trichotillomania. *J. Nurs. Scholarsh.* **2003**, *35*, 165–170. [CrossRef]
30. Keuthen, N.J.; Fama, J.; Altenburger, E.A.; Allen, A.; Raff, A.; Pauls, D. Family environment in adolescent trichotillomania. *J. Obs.-Compuls. Relat. Dis.* **2013**, *2*, 366–374. [CrossRef]
31. American Psychological Association. What Is Cognitive Behavioral Therapy? Available online: <https://www.apa.org/ptsd-guideline/patients-and-families/cognitive-behavioral> (accessed on 12 February 2022).

32. Ninan, P.T.; Rothbaum, B.O.; Marsteller, F.A.; Knight, B.T.; Eccard, M.B. A placebo-controlled trial of cognitive-behavioral therapy and clomipramine in trichotillomania. *J. Clin. Psychiatry* **2000**, *61*, 47–50. [CrossRef]
33. van Minnen, A.; Hoogduin, K.A.L.; Keijsers, G.P.J.; Hellenbrand, I.; Hendriks, G.J. Treatment of trichotillomania with behavioral therapy or fluoxetine: A randomized, waiting-list control study. *Arch. Gen. Psychiatry* **2003**, *60*, 517. [CrossRef]
34. Toledo, E.L.; Muniz, E.D.T.; Brito, A.M.C.; Abreu, C.N.; de Tavares, H. Group Treatment for trichotillomania: Cognitive-behavioral therapy versus supportive therapy. *J. Clin. Psychiatry* **2014**, *76*, 7881. [CrossRef]
35. Keijsers, G.P.J.; Maas, J.; van Opdorp, A.; van Minnen, A. Addressing self-control cognitions in the treatment of trichotillomania: A randomized controlled trial comparing cognitive therapy to behaviour therapy. *Cogn. Ther. Res.* **2016**, *40*, 522–531. [CrossRef]
36. Maas, J.; Keijsers, G.P.J.; Rinck, M.; Becker, E.S. Does cognitive bias modification prior to standard brief cognitive behavior therapy reduce relapse rates in hair pulling disorder? A double-blind randomized controlled trial. *J. Soc. Clin. Psychol.* **2018**, *37*, 453–479. [CrossRef]
37. Slikboer, R.; Rehm, I.C.; Lam, S.; Maloney, A.; Nedeljkovic, M. A brief, residential peer-support retreat for trichotillomania: A mixed methods evaluation. *Aust. Psychol.* **2020**, *55*, 169–180. [CrossRef]
38. Golomb, R.; Franklin, M.; Grant, J.; Keuthen, N.; Mansueto, C.; Mouton-Odum, S.; Woods, D. Expert Consensus Treatment Guidelines for Body-Focused Repetitive Behaviors. Available online: <https://www.bfrb.org/resources/expert-consensus-treatment-guidelines-for-body-focused-repetitive-behaviors> (accessed on 23 February 2022).
39. Shareh, H. A preliminary investigation of metacognitive therapy and habit reversal as a treatment for trichotillomania. *Behav. Cog. Psychother.* **2017**, *46*, 1–20. [CrossRef] [PubMed]
40. Woods, D.W.; Wetterneck, C.T.; Flessner, C.A. A controlled evaluation of acceptance and commitment therapy plus habit reversal for trichotillomania. *Behav. Res. Ther.* **2006**, *44*, 639–656. [CrossRef] [PubMed]
41. Rogers, K.; Banis, M.; Falkenstein, M.J.; Malloy, E.J.; McDonough, L.; Nelson, S.O.; Rusch, N.; Haaga, D.A.F. Stepped care in the treatment of trichotillomania. *J. Consult. Clin. Psychol.* **2014**, *82*, 361–367. [CrossRef] [PubMed]
42. Dougherty, D.D.; Loh, R.; Jenike, M.A.; Keuthen, N.J. Single modality versus dual modality treatment for trichotillomania: Sertraline, behavioral therapy, or both? *J. Clin. Psychiatry* **2006**, *67*, 1086–1092. [CrossRef] [PubMed]
43. Twohig, M.P.; Woods, D.W. A preliminary investigation of acceptance and commitment therapy and habit reversal as a treatment for trichotillomania. *Behav. Ther.* **2004**, *35*, 803–820. [CrossRef]
44. Moritz, S.; Penney, D.; Ahmed, K.; Schmotz, S. A head-to-head comparison of three self-help techniques to reduce body-focused repetitive behaviors. *Behav. Modif.* **2021**, *46*, 014544552110107. [CrossRef] [PubMed]
45. Association for Contextual Behavioral Science. Acceptance and Commitment Therapy. Available online: <https://contextualscience.org/act> (accessed on 3 March 2022).
46. Lee, E.B.; Homan, K.J.; Morrison, K.L.; Ong, C.W.; Levin, M.E.; Twohig, M.P. Acceptance and commitment therapy for trichotillomania: A controlled trial of adults and adolescents. *Behav. Modif.* **2013**, *44*, 70–91. Available online: <https://pubmed.ncbi.nlm.nih.gov/30117327/> (accessed on 14 May 2022). [CrossRef]
47. Crosby, J.M.; Dehlin, J.P.; Mitchell, P.R.; Twohig, M.P. Acceptance and commitment therapy and habit reversal training for the treatment of trichotillomania. *Cogn. Behav. Pract.* **2012**, *19*, 595–605. [CrossRef]
48. Moritz, S.; Rufer, M. Movement decoupling: A self-help intervention for the treatment of trichotillomania. *J. Behav. Ther. Exper. Psychiatry* **2011**, *42*, 74–80. [CrossRef]
49. Weidt, S.; Klaghofer, R.; Kuenburg, A.; Bruehl, A.B.; Delsignore, A.; Moritz, S.; Rufer, M. Internet-based self-help for trichotillomania: A randomized controlled study comparing decoupling and progressive muscle relaxation. *Psychother. Psychosom.* **2015**, *84*, 359–367. [CrossRef]
50. Lebow, J. Overview of Psychotherapies. Available online: <https://www.uptodate.com/contents/overview-of-psychotherapies/print> (accessed on 24 April 2022).
51. Keuthen, N.J.; Rothbaum, B.O.; Welch, S.S.; Taylor, C.; Falkenstein, M.; Heekin, M.; Jordan, C.A.; Timpano, K.; Meunier, S.; Fama, J.; et al. Pilot trial of dialectical behavior therapy-enhanced habit reversal for trichotillomania. *Depress. Anxiety* **2010**, *27*, 953–959. [CrossRef] [PubMed]
52. Keuthen, N.J.; Rothbaum, B.O.; Falkenstein, M.J.; Meunier, S.; Timpano, K.R.; Jenike, M.A.; Welch, S.S. DBT-enhanced habit reversal treatment for trichotillomania: 3-and 6-month follow-up results. *Depress. Anxiety* **2010**, *28*, 310–313. [CrossRef] [PubMed]
53. Keuthen, N.J.; Rothbaum, B.O.; Fama, J.; Altenburger, E.; Falkenstein, M.J.; Sprich, S.; Kearns, M.C.; Meunier, S.; Jenike, M.A.; Welch, S.S. DBT-enhanced cognitive-behavioral treatment for trichotillomania: A randomized controlled trial. *J. Behav. Addict.* **2012**, *1*, 106–114. [CrossRef] [PubMed]
54. Chokhawala, K.; Stevens, L. Antipsychotic medications. In *StatPearls*; StatPearls: Tampa, FL, USA, 2023. Available online: <https://www.ncbi.nlm.nih.gov/books/NBK519503/> (accessed on 14 March 2023).
55. Van Ameringen, M.; Mancini, C.; Oakman, J.M.; Farvolden, P. The potential role of haloperidol in the treatment of trichotillomania. *J. Affect. Disord.* **1999**, *56*, 219–226. [CrossRef] [PubMed]
56. Stein, D.J.; Hollander, E. Low-dose pimozide augmentation of serotonin reuptake blockers in the treatment of trichotillomania. *J. Clin. Psychiatry* **1992**, *53*, 123–126. Available online: <https://pubmed.ncbi.nlm.nih.gov/1532960/> (accessed on 22 May 2022). [PubMed]
57. Stewart, R.S.; Nejtcek, V.A. An open-label, flexible-dose study of olanzapine in the treatment of trichotillomania. *J. Clin. Psychiatry* **2003**, *64*, 49–52. [CrossRef] [PubMed]

58. Van Ameringen, M.; Mancini, C.; Patterson, B.; Bennett, M.; Oakman, J. A randomized, double-blind, placebo-controlled trial of olanzapine in the treatment of trichotillomania. *J. Clin. Psychiatry* **2010**, *71*, 1336–1343. [[CrossRef](#)] [[PubMed](#)]
59. Stein, D.J.; Bouwer, C.; Hawkrigde, S.; Emsley, R.A. Risperidone augmentation of serotonin reuptake inhibitors in obsessive compulsive and related disorders. *J. Clin. Psychiatry* **1997**, *58*, 119–122. [[CrossRef](#)]
60. Epperson, C.N.; Fasula, D.; Wasylinski, S.; Pride, L.H.; McDougale, J. Risperidone addition in serotonin reuptake inhibitor-resistant trichotillomania: Three cases. *J. Child Adolesc. Psychopharmacol.* **1999**, *9*, 43–49. [[CrossRef](#)]
61. Oravec, R.; Štuhec, M. Trichotillomania successfully treated with risperidone and naltrexone: A geriatric case report. *J. Am. Med. Dir. Assoc.* **2014**, *15*, 301–302. [[CrossRef](#)]
62. White, M.P.; Koran, L.M. Open-label trial of aripiprazole in the treatment of trichotillomania. *J. Clin. Psychopharmacol.* **2011**, *31*, 503–506. [[CrossRef](#)] [[PubMed](#)]
63. Moraczewski, J.; Awosika, A.O.; Aedma, K.K. Tricyclic antidepressants. In *StatPearls*; StatPearls: Tampa, FL, USA, 2023. Available online: <https://www.ncbi.nlm.nih.gov/books/NBK557791/#:~:text=TCAs%20have%20the%20potential%20to> (accessed on 15 September 2023).
64. Woods, D.W.; Houghton, D.C. Diagnosis, evaluation, and management of trichotillomania. *Psychiatr. Clin. N. Am.* **2014**, *37*, 301–317. [[CrossRef](#)] [[PubMed](#)]
65. Swedo, S.E.; Leonard, H.L.; Rapoport, J.L.; Lenane, M.C.; Goldberger, E.L.; Cheslow, D.L. A double-blind comparison of clomipramine and desipramine in the treatment of trichotillomania (Hair Pulling). *N. Eng. J. Med.* **1989**, *321*, 497–501. [[CrossRef](#)] [[PubMed](#)]
66. Pollard, C.A.; Ibe, I.O.; Krojanker, D.N.; Kitchen, A.D.; Bronson, S.S.; Flynn, T.M. Clomipramine treatment of trichotillomania: A follow-up report on four cases. *J. Clin. Psychiatry* **1991**, *52*, 128–130. Available online: <https://pubmed.ncbi.nlm.nih.gov/2005076/> (accessed on 24 May 2022). [[PubMed](#)]
67. Christenson, G.A.; Mackenzie, T.B.; Mitchell, J.E.; Callies, A.L. A placebo-controlled, double-blind crossover study of fluoxetine in trichotillomania. *Am. J. Psychiatry* **1991**, *148*, 1566–1571. [[CrossRef](#)] [[PubMed](#)]
68. Streichenwein, S.M.; Thornby, J.I. A long-term, double-blind, placebo-controlled crossover trial of the efficacy of fluoxetine for trichotillomania. *Am. J. Psychiatry* **1995**, *152*, 1192–1196. [[CrossRef](#)]
69. Koran, L.M.; Ringold, A.; Hewlett, W. Fluoxetine for trichotillomania: An open clinical trial. *Psychopharmacol. Bull.* **1992**, *28*, 145–149. Available online: <https://pubmed.ncbi.nlm.nih.gov/1513916/> (accessed on 25 May 2022). [[PubMed](#)]
70. Winchel, R.M.; Jones, J.S.; Stanley, B.; Molcho, A.; Stanley, M. Clinical characteristics of trichotillomania and its response to fluoxetine. *J. Clin. Psychiatry* **1992**, *53*, 304–308. Available online: <https://pubmed.ncbi.nlm.nih.gov/1517191/> (accessed on 25 May 2022). [[PubMed](#)]
71. Iancu, I.; Weizman, A.; Kindler, S.; Sasson, Y.; Zohar, J. Serotonergic drugs in trichotillomania: Treatment results in 12 patients. *J. Nerv. Men. Dis.* **1996**, *184*, 641–644. [[CrossRef](#)]
72. Christenson, G.A.; Crow, S.J.; Mitchell, J.E.; Mackenzie, T.B.; Crosby, R.D.; Falls, J. Fluvoxamine in the Treatment of Trichotillomania: An 8-Week, Open-Label Study. *CNS Spectr.* **1998**, *3*, 64–71. [[CrossRef](#)]
73. Stanley, M.A.; Breckenridge, J.K.; Swann, A.C.; Freeman, E.B.; Reich, L. Fluvoxamine treatment of trichotillomania. *J. Clin. Psychopharmacol.* **1997**, *17*, 278–283. [[CrossRef](#)] [[PubMed](#)]
74. Stein, D.J.; Bouwer, C.; Maud, C.M. Use of the selective serotonin reuptake inhibitor citalopram in treatment of trichotillomania. *Eur. Arch. Psychiatry Clin. Neurosci.* **1997**, *247*, 234–236. [[CrossRef](#)]
75. Gadde, K.M.; Wagner, H.R., II; Connor, K.M.; Foust, M.S. Escitalopram treatment of trichotillomania. *Int. Clin. Psychopharmacol.* **2007**, *22*, 39–42. [[CrossRef](#)] [[PubMed](#)]
76. Porton, B.; Greenberg, B.D.; Askland, K.; Serra, L.M.; Gesmonde, J.; Rudnick, G.; Kao, H.-T. Isoforms of the neuronal glutamate transporter gene, SLC1A1/EAAC1, negatively modulate glutamate uptake: Relevance to obsessive-compulsive disorder. *Transl. Psychiatry* **2013**, *3*, e259. [[CrossRef](#)] [[PubMed](#)]
77. Grant, J.E.; Odlaug, B.L.; Won Kim, S. N-Acetylcysteine, a glutamate modulator, in the treatment of trichotillomania. *Arch. Gen. Psychiatry* **2009**, *66*, 756. [[CrossRef](#)] [[PubMed](#)]
78. Vieira, G.d.L.T.; Lossie, A.C.; Lay, D.C.; Radcliffe, J.S.; Garner, J.P. Preventing, treating, and predicting barbering: A fundamental role for biomarkers of oxidative stress in a mouse model of trichotillomania. *PLoS ONE* **2017**, *12*, e0175222. [[CrossRef](#)] [[PubMed](#)]
79. Braun, T.L.; Patel, V.; DeBord, L.C.; Rosen, T. A review of n-acetylcysteine in the treatment of grooming disorders. *Int. J. Dermatol.* **2019**, *58*, 502–510. [[CrossRef](#)] [[PubMed](#)]
80. Rodrigues-Barata, A.; Rodríguez-Pichardo, A.; Tosti, A.; Camacho-Martínez, F. N-acetylcysteine in the treatment of trichotillomania. *Int. J. Trichology* **2012**, *4*, 176. [[CrossRef](#)] [[PubMed](#)]
81. Leppink, E.W.; Redden, S.A.; Grant, J.E. A double-blind, placebo-controlled study of inositol in trichotillomania. *Int. Clin. Psychopharmacol.* **2017**, *32*, 107–114. [[CrossRef](#)]
82. Fux, M.; Levine, J.; Aviv, A.; Belmaker, R.H. Inositol treatment of obsessive-compulsive disorder. *Am. J. Psychiatry* **1996**, *153*, 1219–1221. [[CrossRef](#)]
83. Seedat, S.; Stein, D.J.; Harvey, B.H. Inositol in the Treatment of Trichotillomania and Compulsive Skin Picking. *J. Clin. Psychiatry* **2001**, *62*, 60–61. [[CrossRef](#)] [[PubMed](#)]
84. Cleveland Clinic. Opioid Antagonist. Available online: <https://my.clevelandclinic.org/health/treatments/24878-opioid-antagonist> (accessed on 4 January 2024).

85. Grant, J.E.; Odlaug, B.L.; Schreiber, L.; Kim, S.W. The opiate antagonist, naltrexone, in the treatment of trichotillomania. Results of a double blind, placebo-controlled study. *J. Clin. Psychopharmacol.* **2014**, *34*, 134–138. [[CrossRef](#)]
86. O'Donnell, B.; Meissner, H.; Gupta, V. Dronabinol. In *StatPearls*; StatPearls: Tampa, FL, USA, 2023. Available online: <https://www.ncbi.nlm.nih.gov/books/NBK557531/> (accessed on 19 January 2024).
87. Herkenham, M.; Lynn, A.B.; Little, M.D.; Johnson, M.R.; Melvin, L.S.; de Costa, B.R.; Rice, K.C. Cannabinoid receptor localization in the brain. *Proc. Natl. Acad. Sci. USA* **1990**, *87*, 1932–1936. [[CrossRef](#)] [[PubMed](#)]
88. Grant, J.E.; Odlaug, B.L.; Chamberlain, S.R.; Kim, S.W. Dronabinol, a cannabinoid agonist, reduces hair pulling in trichotillomania: A pilot study. *Psychopharmacology* **2011**, *218*, 493–502. [[CrossRef](#)] [[PubMed](#)]
89. Grant, J.E.; Valle, S.; Chesivoir, E.; Ehsan, D. Tetrahydrocannabinol fails to reduce hair pulling and skin picking: Results of a double-blind, placebo-controlled study of dronabinol. *Int. J. Clin. Psychopharmacol.* **2022**, *37*, 14–20. [[CrossRef](#)] [[PubMed](#)]
90. Dos Santos Tenório, M.C.; Graciliano, N.G.; Moura, F.A.; de Oliveira, A.C.M.; Goulart, M.O.F. N-Acetylcysteine (NAC): Impacts on human health. *Antioxidants* **2021**, *10*, 967. [[CrossRef](#)] [[PubMed](#)]
91. Cleveland Clinic. What Is Inositol? Available online: <https://my.clevelandclinic.org/health/drugs/25173-inositol> (accessed on 30 October 2023).
92. Moritz, S.; Gallinat, C.; Weidinger, S.; Bruhns, A.; Lion, D.; Snorrason, I.; Keuthen, N.; Schmotz, S.; Penney, D. The generic BFRB scale-8 (GBS-8): A transdiagnostic scale to measure the severity of body-focused repetitive behaviors. *Behav. Cogn. Psychother.* **2022**, *50*, 620–628. [[CrossRef](#)]
93. Winchel, R.M.; Jones, J.S.; Molcho, A.; Parsons, B.; Stanley, B.; Stanley, M. The psychiatric institute trichotillomania scale (PITS). *Psychopharmacol. Bull.* **1992**, *28*, 463–476. Available online: <https://pubmed.ncbi.nlm.nih.gov/1296224/> (accessed on 30 October 2023).

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.