The phenomenon of hair pulling has been recognized for centuries, yet the true prevalence of trichotillomania (TTM) is largely unknown and the topic has been sparsely studied. TTM is classified as an impulse-control disorder despite much debate about its etiology. In this review we summarize the different hypotheses, including impulse-control disorders, obsessive-compulsive disorders, behavioral problems and addiction, and the appropriate treatment methods. The combination of selective serotonin reuptake inhibitors and antipsychotic medications are shown to be most effective. Treatment with anti-addiction drugs seems relevant. Further research is needed to increase our knowledge regarding the etiology of TTM.

In addition, the pulling must not be accounted for by another psychiatric or medical condition [5]. Although the DSM-IV definition requires all of the above criteria, it is plausible that not all of the characteristics are present in all clinically significant cases. It is reported that 17%–27% of patients do not complain of rising tension before, during or after the hair pulling. In addition, clinical cases show that the pulling of hair does not necessarily cause hair loss or distress, implying that the behavior occurs on a continuum, ranging from unnoticeable to disfiguring [4]. Therefore, the DSM criteria for the diagnosis of TTM might be overly restrictive and prevents suffering individuals from getting the help they need [2-5].

Due to the inconsistencies in diagnostic criteria, the true prevalence of TTM is largely unknown. The prevalence of TTM varies between different studies, ranging from a lifetime prevalence of 0.6% using the DSM-IV criteria, to 4% of the general population, and 10% having had the habit at some point in their lives. By the time the correct diagnosis is made, it is not uncommon for a patient to have been diagnosed with and already treated for other medical conditions such as tinea capitis or alopecia areata [1,6-8].

Gender distribution in the general population is also uncertain, but in the clinical setting there is a higher prevalence among women [9]. This may be explained by the fact that women are more inclined to seek help, that men may blame male pattern baldness, or that men have the advantage of shaving their heads and beards with little resultant social stigma [4]. However, additional data on the differences between men and women might allude to an actual bias in gender. For example, the age at onset of hair pulling was significantly later for males [8] than for females [10-12]. In addition, there are significantly more males than females who present with comorbid obsessive-compulsive disorder and tics. Males and females also differed in terms of the hair pulling site (men pull hair from the stomach/back and the moustache/beard areas, while women pull from the scalp) [10].

Three subtypes of hair pulling have been distinguished [4]:

- **Early onset**, considered the benign form of TTM, occurring in young children (under the age of 8), which receives little attention from the medical community. In general, early onset TTM is more common than thought.

- **Late onset**, characterized by a higher age of onset, usually in adolescence or adulthood. The behavior often persists for many years and can be associated with significant distress.

- **Somatization TTM**, which is characterized by the presence of physical symptoms, such as headaches, stomachaches, or other complaints, that are not explained by any medical condition.

Trichotillomania is more common than thought. In the general population, the prevalence of TTM varies between different studies, ranging from a lifetime prevalence of 0.6% using the DSM-IV criteria, to 4% of the general population, and 10% having had the habit at some point in their lives. By the time the correct diagnosis is made, it is not uncommon for a patient to have been diagnosed with and already treated for other medical conditions such as tinea capitis or alopecia areata [1,6-8].
to no medical intervention. It is believed that the pattern of anxiety and tension followed by relief is not present in this form of TTM.

- **Automatic**, thought to occur when the individual is engaged in other activities, such as reading, watching television, listening to the radio, etc., and affects roughly 75% of TTM patients.
- **Focused**, thought to occupy the individual’s attention, and is associated with more intense urges and thoughts about hair pulling, alluding to the comparison between this subtype of TTM and obsessive-compulsive disorders.

Automatic and focused TTM are usually not exclusive and vary, overlap or co-occur [4]. Still, focused TTM is defined as pulling with a compulsive quality, which may represent an attempt to regulate negative emotions [9].

TTM may cause additional physical impairments and distress; sucking and chewing of the pulled hair is observed in 48% of patients, and 5%–18% of patients ingest the pulled hair. In addition, skin infections, scalp bleeding or irritation, and carpal tunnel syndrome are also prevalent in TTM patients. In the social dimension, 22–63% of TTM patients report avoidance of common activities. The feeling of isolation and loneliness is common, as are feelings of shame and embarrassment. TTM patients tend to have low self-esteem, feelings of unattractiveness, and body dissatisfaction. The use of legal and illegal drugs to cope with those feelings has been reported [4]. People suffering from TTM will commonly deny the condition and may become adept at disguising their hair loss [5].

Psychiatric comorbidity is common, with one or more lifetime psychiatric diagnoses found in 82%, major depression in 37–65%, anxiety disorder in 55–60%, and excessive alcohol use in 33% [11].

### ETIOLOGY AND TREATMENT THEORIES

Although TTM is classified in the DSM-IV-TR [2] and in the ICD-10 [3] as an impulse-control disorder, there has been much debate regarding the etiology of this disorder. Hair-pulling behaviors have been observed in animals, such as rabbits, sheep, dogs, cats and others; and the analogue behavior of feather-picking has also been noted in birds [4]. Thus, TTM behavior is thought to be an inappropriately triggered grooming behavior [12].

**Trichotillomania affects primarily females in every age group**

OCD = obsessive-compulsive disorder

SSRIs = selective serotonin reuptake inhibitors

**OCD SPECTRUM ETIOLOGY AND SSRI TREATMENT**

It has been suggested that TTM belongs to the OCD spectrum and that the use of selective serotonin reuptake inhibitors could benefit the sufferers. It is believed by some researchers that OCD and TTM share overlapping comorbidity, familial transmission and possibly treatment response. Both OCD and TTM are characterized by repetitive, intentionally performed behaviors that cause significant distress or functional impairment [13]. Although the repetitive behavior of TTM exclusively involves hair pulling, this behavior often follows high anxiety and results in reduced anxiety [14]. In addition, whole-brain magnetic resonance imaging showed that medication-free TTM patients had increased gray matter in the left putamen and multiple cortical regions, similar to the increase in Tourette syndrome and in OCD [15]. In a different study, TTM patients were found to have smaller left putamen volumes than matched controls, thus providing evidence for a link between TTM and Tourette syndrome. Furthermore, TTM patients present with reduced volumes for the total right and left cerebellum cortex, as well as for the autonomic/emotional functional cluster compared with controls [16].

The hypothesis of an OCD spectrum origin of TTM led to the use of SSRIs as a treatment option. However, studies on the potency of SSRIs in TTM have yielded mixed results [17]. According to various studies from the 1990s [18-21], SSRI and other antidepressants improve some aspects of TTM, although placebo-controlled trials have not shown consistent results. In a study in 2007, some patients with TTM experienced significant improvement after treatment with escitalopram [22]. In a 2003 study, fluoxetine was found ineffective for the treatment of TTM [23]; however, in another study, conducted in 1991, it was not more effective than a placebo [24]. In two studies, one in 1996 and the other in 2000, clomipramine was also found to be ineffective for the treatment of TTM [25,26].

An explanation for the SSRI lack of success in treating TTM might be found in the core assumption that led to the use of SSRIs in the first place. Although TTM and OCD share some common ground, there are fundamental differences between the two disorders. For example, in contrast to compulsions in OCD, hair pulling in TTM is not a response to obsessive thoughts but is due to an irresistible urge and the promise of gratification after the hair pulling. Also, unlike patients with OCD whose symptoms change over time in terms of focus and severity, TTM patients usually present with hair pulling without evolution to non-self-injurious compulsive rituals [9]. Moreover, there are no obsessions preceding the compulsions.

With regard to demographic variables, TTM is far more prevalent in females, whereas OCD is equally common in both genders, and while TTM typically presents an early onset in adolescence, OCD usually appears in childhood through early adulthood [9].

Other clinical observations point to a difference in characterization between the two disorders. Patients suffering from TTM present fewer comorbid obsessive-compulsive symptoms,
as well as less depression and anxiety compared to symptoms in patients suffering from OCD. When behavioral techniques such as response prevention are applied in patients suffering from OCD, it eventually leads to anxiety reduction, whereas in people with TTM it may lead to an increase in anxiety. Additional clinical observations included more sexual abuse and more maladaptive cognitive schemas reported by OCD patients, while TTM patients were more novelty seeking [9].

BEHAVIORAL ETIOLOGY AND COGNITIVE BEHAVIORAL THERAPY
It has been proposed that TTM occurs through a learning process, similar to the formation of habits [4], and that it might resemble the habit of thumb sucking or nail biting [5]. It may also develop as a coping behavior in response to stress and is reinforced through tension reduction [4]. Habit-reversal training is the preferred behavioral treatment for TTM; it involves three primary components: a) awareness training, b) competing response trainings, and c) social support. Other techniques have been incorporated into the habit-reversal training routine, such as stimulus control, cognitive restructuring, relaxation training and thought stopping [9].

The application of behavioral therapy is rooted in learning theories. By interrupting the chain of conditioned and discriminated stimuli, urges, hair-pulling behavior and gratification following hair pulling, classical and operant conditioning of hair-pulling behavior weakens over time [8,10].

One study reports these types of treatments to be more useful for the treatment of TTM than pharmacotherapy [9]. In another study conducted in 2000, cognitive behavioral therapy had a dramatic effect and achieved statistical significance in reducing TTM symptoms compared to SSRIs and placebos [26]. The results from a 2003 study are similar to other studies, showing that behavioral therapy is superior to both fluoxetine treatment and postponement of treatment, and 64% of patients in the CBT group showed a significant reduction in the severity of TTM, including actual hair pulling [23]. In a 2006 study, TTM abated considerably immediately after brief behavioral therapy [27]; in a study from 2007, habit-reversal training was found to be the most effective intervention for TTM when practiced by experienced clinicians in academic research settings, compared to pharmacotherapy [28].

However, despite positive results, the effectiveness of behavioral and cognitive strategies varies across clients and involves significant risk for relapse [21]. In addition, in a study comparing a single modality approach with CBT and pharmacotherapy to a dual modality approach using the two treatments combined, the dual modality was found to be slightly more effective [29].

Although data on the psychological and pharmacological treatments of trichotillomania are incomplete, cognitive behavioral therapy and opioid antagonist pharmacotherapy yielded the most promising results.

ANTIPSYCHOTIC PHARMACOTHERAPY AND DOPAMINE THEORY
Although the role of serotonin has been postulated in TTM and other impulse-control disorders, the use of SSRIs in the treatment of TTM has proven inadequate. One possibility for this shortcoming might be the involvement of other pathways and neurotransmitters, such as opioids and dopamine [30].

In a case report from 2008, pharmacotherapy with fluoxetine led to intolerable side effects. However, when quetiapine was introduced at a dosage of 100 mg/week, both hair pulling and fluoxetine side effects remitted. Cessation of hair pulling lasted for a period of 4 months. This report sheds new light on the combination of SSRIs with antipsychotic medications as a treatment modality for TTM [30]. Yet, in another study conducted in 2008, the use of aripiprazole was associated with the rapid and sustained cessation of hair pulling [11]. The efficacy of the combination of SSRIs and antipsychotic agents has yet to be elucidated.

ADDICTIVE SPECTRUM AND REWARD CIRCUIT THEORY
Although the similarities between TTM and OCD have been suggested and studied extensively in recent years, many features of TTM are also common with addictive disorders. First, the repetitive or compulsive engagements, despite adverse consequences, which are the core of TTM, resemble the nature of addiction. Patients suffering from TTM also exhibit, as in other addictions, diminished control over their problematic behavior, a growing craving prior to engaging in the problematic behavior, and lastly, a gratification during and after engaging in the problematic behavior. An important difference between compulsions in OCD and hair pulling in TTM is that hair pulling and addiction are usually accompanied by pleasurable or rewarding feelings, while compulsions are executed to decrease anxiety [31].

Reinforcement for the addiction spectrum hypothesis can be found in case reports and studies testing the efficacy of the medications on dopaminergic and serotonergic neurotransmitters in TTM. In a case report from 2004, patients treated with bupropion at a dosage of 150 mg twice daily noted almost complete remission of TTM symptoms. It is hypothesized that bupropion decreases TTM symptoms by diminishing the heightened arousal and pleasurable relief that are involved in hair pulling [32]. Dannon et al. [33] recently completed a study with bupropion XR in the treatment of TTM, showing significant improvement at the 12 week point [33].

OTHER TREATMENT POSSIBILITIES: MOOD STABILIZERS AND FOOD SUPPLEMENTS
Another study found significant reduction in hair pulling following the use of topiramate, which is an antiepileptic drug
known to be effective in the treatment of other impulse-control disorders [10,34]. The use of lamotrigine, a mood stabilizer, also appears to have significant effect in treating TTM [35], as did the mood stabilizer oxcarbazepine [36]. N-acetylcysteine, a glutamate modulator (food supplement), was also shown to be effective in TTM on the primary and secondary outcome measures. Its beneficial effects were seen 9 weeks after treatment initiation [37].

**ETIOLOGY AND GENETIC THEORIES**

Genetic factors appear to contribute to the development of TTM. A significantly different concordance rate for TTM was found in monozygotic (38.1%) compared with dizygotic (0%) twins in 34 pairs [38]. Several researchers found mutations of the *SLITRK1* gene, which plays a role in cortex development and neuronal growth [39]. Zuckner and colleagues [39] also found that a heterozygous variant of postsynaptic synapse-associated protein 90/postsynaptic density-95-associated protein (SAPAP)3, which is involved in the excitatory transmissions at corticostriatal synapses, was present in only 1.1% of the controls, compared with 4.2% of those diagnosed with TTM and OCD. Researchers suggest that SAPAP3 may be involved in the development of obsessive-compulsive spectrum disorders.

**ETIOLOGY AND NEUROCOGNITIVE NEUROIMAGING THEORIES**

Several authors measured impulsivity with the Stop Signal Task and demonstrated an impaired inhibitory control; however, other studies using the Wisconsin Card Sorting test and the go/no-go task found no significant differences between TTM patients and normal controls [40].

Few brain imaging studies have been performed, and these were with a relatively small number of TTM patients. These studies showed a wide range from no difference to an increased gray matter density in the striatum, left amygdalo-hippocampal formation, and multiple cortical regions.

**DISCUSSION**

The phenomena of hair pulling, termed trichotillomania, is unique due to the controversy revolving around its etiology and optimal treatment. Officially, and according to the DSM-IV [2] and the ICD-10 [3], TTM is categorized as an impulse-control disorder.

Due to the lack of success in treating TTM fully, other explanations regarding the etiology of TTM have been proposed, followed by treatment propositions. Chamberlain [1,6] and others have suggested that TTM is a part of the OCD spectrum, and therefore they treated TTM patients with SSRIs; this method has proven to be only partially effective [24].

A different suggestion attributed TTM to the behavioral disorders spectrum, and accordingly used CBT as the treatment method [10,35]. However, as with SSRIs, the use of CBT did not yield satisfying results [3,9,10,27,30].

The use of dopamine-related medications in TTM patients was chosen due to the opioid and dopamine involvement in the disorder [7]. To date, there have not been sufficient studies to clearly demonstrate the therapeutic effects of these medications. Other treatments, such as mood stabilizers and food supplements, were shown to be somewhat effective but require further larger studies.

Our group has been studying the effect of dopaminergic medications in TTM patients (bupropion sustained release and naltrexone) due to the similarities between the two disorders. A few studies have found these medications to be the most useful for treating TTM [1,15].

**CONCLUSIONS**

TTM is much more common than believed and seems to be much more complex than the easily categorized impulse-control disorder. Although TTM shares similarities with the OCD spectrum, the matching treatment possibilities, such as SSRIs, were proven less effective in TTM. The hypotheses of dopamine, glutamate or GABA (gamma-aminobutyric acid) in TTM have underlined the use of mood stabilizers, antipsychotic and dopamine-related drugs. Currently, CBT seems to be the treatment of choice in psychotherapeutic interventions. To date, the most promising results have been evident when CBT and opioid antagonist pharmacotherapy were implemented.

**Corresponding author:**
**Dr. P.N. Dannon**

Research Department, Beer Yaakov Mental Health Hospital, P.O. Box 1, Beer Yaakov 60350, Israel

**Phone:** (972-8) 925-8252

**Fax:** (972-8) 921-2570

**email:** pinhasd@post.tau.ac.il

**References**


**New gene functions in megakaryopoiesis and platelet formation**

Platelets are the second most abundant cell type in blood and are essential for maintaining hemostasis. Their count and volume are tightly controlled within narrow physiological ranges, but there is only limited understanding of the molecular processes controlling both traits. Gieger and co-researchers carried out a high powered meta-analysis of genome-wide association studies (GWAS) in up to 66,867 individuals of European ancestry, followed by extensive biological and functional assessment. The authors identified 68 genomic loci reliably associated with platelet count and volume mapping to established and putative novel regulators of megakaryopoiesis and platelet formation. These genes show megakaryocyte-specific gene expression patterns and extensive network connectivity. Using gene silencing in *Danio rerio* and *Drosophila melanogaster*, they identified 11 of the genes as novel regulators of blood cell formation. Taken together, their findings advance understanding of novel gene functions controlling fate-determining events during megakaryopoiesis and platelet formation, providing a new example of successful translation of GWAS to function.