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## REVIEW ARTICLE

# Trichotillomania is more related to Tourette disorder than to obsessive-compulsive disorder

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**Objective:** Trichotillomania (TTM) is characterized by the pulling out of one's hair. TTM was classified as an impulse control disorder in DSM-IV, but is now classified in the obsessive-compulsive related disorders section of DSM-5. Classification for TTM remains an open question, especially considering its impact on treatment of the disorder. In this review, we questioned the relation of TTM to tic disorder and obsessive-compulsive disorder (OCD).

**Method:** We reviewed relevant MEDLINE-indexed articles on clinical, neuropsychological, neurobiological, and therapeutic aspects of trichotillomania, OCD, and tic disorders.

**Results:** Our review found a closer relationship between TTM and tic disorder from neurobiological (especially imaging) and therapeutic standpoints.

**Conclusion:** We sought to challenge the DSM-5 classification of TTM and to compare TTM with both OCD and tic disorder. Some discrepancies between TTM and tic disorders notwithstanding, several arguments are in favor of a closer relationship between these two disorders than between TTM and OCD, especially when considering implications for therapy. This consideration is essential for patients.

**Keywords:** Obsessive-compulsive disorder; trichotillomania; Tourette syndrome; tic disorders; psychiatry

## Introduction

As its name implies, obsessive-compulsive disorder (OCD) is defined by obsessions and compulsions.<sup>1</sup> Obsessions are thoughts, images, or urges experienced as unwanted and which cause marked anxiety; compulsions are repetitive behaviors performed to prevent or reduce the anxiety caused by obsessions.<sup>1</sup> In DSM-IV-TR, this disorder was classified within the anxiety disorders,<sup>2</sup> but now, in DSM-5, OCD is included in a specific group called "obsessive-compulsive and related disorder."<sup>1</sup> This group also includes body dysmorphic disorder and trichotillomania (TTM).<sup>1</sup> TTM is defined by recurrent pulling out of one's hair, resulting in hair loss,<sup>1</sup> and was classified as an impulse control disorder in DSM-IV-TR.<sup>2</sup> A third disorder – or, rather a group of disorders – is that of tic disorders, which have been linked to OCD in several aspects.<sup>3-8</sup> A tic is a sudden, rapid, recurrent, nonrhythmic motor movement or vocalization.<sup>1</sup> Some types of tics, especially complex ones, could in fact be considered symptoms of OCD, and some OCD symptoms could conversely be considered complex tics.<sup>9</sup>

Lochner et al.<sup>10</sup> have examined the tic disorders vs. OCD relationship, which includes other complex repetitive behaviors, particularly TTM. Evaluating lifetime comorbidities, degree of disability, and response to treatment, these authors noted significant differences between OCD and TTM, and reached the conclusion that these two disorders were obviously different; furthermore, they reached the conclusion that TTM was wrongly classified as an impulse control disorder. But is "obsessive-compulsive related disorder" a better classification for TTM? A review questioning the content of an eventual obsessive-compulsive spectrum grouping of disorders stated that TTM would be better placed in a group of body-focused repetitive disorders than in that of obsessive-compulsive related disorders, unless the former group were not included in DSM-5.<sup>11</sup> And even if TTM were to be classified as an obsessive-compulsive related disorder (as it ultimately was), the authors stated that the overlap between OCD and TTM would be "partial at best."<sup>11</sup> But what about TTM and tics? Would the tic disorders group be a better group for TTM? Is TTM in fact a complex tic rather than a compulsion?

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In this critical review, we will consider different aspects of OCD, tic disorders, and TTM to discuss the possibility of a closer relationship between TTM and tic disorders than between TTM and OCD.

It is worth noting that Tourette syndrome (TS) has been the subject of much more research than simple tic disorders; we will thus refer much more often to TS than to the latter.

## Method

Our research question was the following: could TTM be considered a tic disorder rather than an obsessive-compulsive related disorder? To carry out our critical review and answer this question, we searched the MEDLINE database (via PubMed) on November 2018.

We conducted this search across five axes we considered relevant: phenomenological investigation of urges, comorbidities, neuropsychology (especially attention, inhibition, working memory, and flexibility), imaging, and pharmacology. The inclusion criteria were as follows:

- Only original studies were considered (case reports, qualitative studies, and qualitative reviews were thus excluded, except for the “antipsychotics and TTM” part, as we found very few original studies);
- If meta-analyses existed, we considered only the meta-analysis and not the original studies cited therein;
- The reviewed studies should be written in English only;
- The populations studied in original research should be patients with OCD, TTM, or tic disorders;
- The selected studies should specifically include results concerning the field of interest.

### *Terms used in the search*

The PubMed search queries used for each of the different axes are described below.

#### Phenomenology

The search query “urges AND (OCD OR “obsessive-compulsive disorder”)” yielded 122 results; “urges AND Tourette,” 124 results; and “urges AND (trichotillomania OR “hair pulling disorder”)” returned 28 results.

Among the OCD results, we found 22 articles potentially relevant for our aim. After full-text reading, 12 of these articles were found to assess OCD phenomenology and thus selected for further analysis (Table 1). Among the articles identified by the urges and TS query, we deemed 78 relevant and selected 20 (Table 1). Finally, among the articles returned by the urges and TTM query, we deemed eight relevant and ultimately selected only two (Table 1).

#### Comorbidity

The search query “(“hair pulling disorder” OR trichotillomania) AND (OCD OR “obsessive-compulsive disorder”) and comorbidity” yielded 81 articles, of which 19 were ultimately selected; “(“hair pulling disorder” or trichotillomania)

and Tourette and comorbidity” yielded 11 articles, of which four studies were ultimately selected (Table 2).

#### Neuropsychology

Considering the huge numbers of articles found in this part concerning OCD, we considered only two well-done meta-analyses: one in adults<sup>12</sup> and one in children.<sup>13</sup>

For TTM, our query was “(TTM or trichotillomania) AND (“working memory” OR “inhibition” OR “attention” OR “flexibility”)”; it returned 181 results, of which 12 were ultimately selected; for TS, “Tourette AND (“working memory” OR “inhibition” OR “attention” OR “flexibility”)” yielded 1,306 results. However, we found a meta-analysis<sup>14</sup> concerning inhibition, and thus excluded this term from our search. The query was then repeated as follows: “Tourette AND (“working memory” OR “inhibition” OR “attention” OR “flexibility”)”, which returned 1,159 results. We found a well-done recent meta-analysis concerning flexibility (through the Wisconsin Card Sorting Test),<sup>15</sup> and thus removed that term from the query as well. Finally, we searched for the terms “Tourette AND (“working memory” OR “attention”)”, which yielded 1,155 records; 11 were ultimately selected (Table 3).

#### Imaging

We found two meta-analyses of voxel-based morphometry (VBM) analysis with magnetic resonance imaging (MRI) in OCD patients.<sup>16,17</sup> For TS, the query was “Tourette AND MRI,” yielding 293 results, of which 11 were ultimately selected. For TTM, our query was “(TTM or trichotillomania) AND MRI,” which yielded 55 results; nine were selected for inclusion (Table 4).

#### Treatment

This final part included six separate queries. The terms “(OCD OR “obsessive-compulsive disorder”) AND (SRI OR “serotonin reuptake inhibitor”)” returned 479 records, 11 of which (all meta-analyses) were ultimately selected. The query “(OCD OR “obsessive-compulsive disorder”) AND (antipsychotic OR neuroleptic)” yielded 985 results, seven of which (again, all meta-analyses) were ultimately selected. “Tourette AND (SRI OR “serotonin reuptake inhibitor”)” returned 15 results, only one of which was selected; “Tourette AND (antipsychotic OR neuroleptic)” yielded 767 results, three of which (all meta-analyses) were selected. The query “(trichotillomania or “hair pulling disorder”) AND (antipsychotic OR neuroleptic)” yielded 61 results. Considering the low number of studies, we decided to include case reports as well; 22 articles were ultimately selected. Finally, “(trichotillomania or “hair pulling disorder”) AND (SRI OR “serotonin reuptake inhibitor”)” yielded 20 results, seven of which were selected (Table 5).

## Clinical comparison of TTM, OCD, and tic disorders

### *Phenomenology*

TTM is defined by DSM-5 as an obsessive-compulsive related disorder.<sup>1</sup> The two main diagnostic criteria are

“recurrent pulling out of one’s hair, resulting in hair loss” and “repeated attempts to decrease or stop hair pulling.”<sup>1</sup> As these diagnostic criteria show, TTM does not involve any obsessions. DSM-5 thus considers TTM as a differential diagnosis of OCD and explains that the one difference from OCD is the absence of obsession in TTM (obsessions are one of the two key diagnostic criteria of OCD, alongside compulsions,<sup>1</sup> even if absence of obsession does not exclude OCD).

The more detailed phenomenology of TTM, as described by DSM-5, involves that hair pulling “may be triggered by feelings of anxiety or boredom (and) may be preceded by an increasing sense of tension (either immediately before pulling out the hair or when attempting to resist the urge to pull).”<sup>1</sup> It is then interesting to notice that some of the phenomenology involved in tics (which are sudden, rapid, recurrent, nonrhythmic motor movements or vocalizations<sup>1</sup>) bears similarities with those of TTM precisions. Indeed, regarding tics, the DSM-5 explains that “as children get older, they begin to report their tics being associated with a premonitory urge – a somatic sensation that precedes the tic – and a feeling of tension reduction following the expression of the tic” and that “tics are worsened by anxiety.”<sup>1</sup> Hence, tics and TTM are both preceded by urges.

Urges are closer to physical sensations, while obsessions are closer to cognitive processes (e.g., thoughts or images). But obsessions also involve urges, as a subtype of obsessions themselves distinct from thoughts or images.<sup>1</sup>

Considering the potential importance of urge phenomena for challenging the DSM-5 classification of TTM, we decided to conduct a systematic review concerning this phenomenon (Table 1).

Articles have reported urges and sensory phenomena in OCD patients,<sup>18-23</sup> with a temporal relationship between these phenomena and the compulsions.<sup>23-25</sup> Urges are defined as being distinct phenomena: sensory phenomena, “just-right” sensations, or other phenomena, e.g., a need for the patient to release energy.<sup>26</sup> Studies were divided regarding the association between “just-right”/incompleteness feelings and OCD severity scales: some found no correlation,<sup>18</sup> while others did.<sup>21</sup> Furthermore, it is interesting to note that OCD patients with sensory phenomena presented symmetry compulsions more frequently than OCD patients without these phenomena.<sup>20</sup> Studies also found that urges (sensory phenomena, aggressive urges, or “just-right” phenomena) were more often present in OCD + TS patients than in OCD-only patients.<sup>19,27,28</sup> These results (concerning symmetry compulsions and OCD-only vs. OCD + TS) are interesting when compared with the finding of Worbe et al. that symmetry or “just-right” phenomena were more often considered tics than compulsions (the difference between tic and compulsion being the nature of the different repetitive behaviors, based on the absence or presence of anxiety, with tics being unrelated to anxiety).<sup>9</sup>

Urges are found in TS patients, with a temporal relationship between tics and urges.<sup>29-37</sup> Furthermore, studies have found that TS patients with urges have more severe tics.<sup>38-43</sup> Considering our aim, it is interesting to note that studies found that urges were associated with symmetry compulsion or “just-right” experiences<sup>21,38,41,44</sup> in TS patients. These findings are similar to those reported for OCD patients above (i.e., urges are more frequent when symmetry compulsions and comorbid tics are present). We can thus remark, as before, that these urges concerned specific repetitive behaviors (not the

**Table 1** Premonitory urges in obsessive-compulsive disorder, Tourette syndrome, and trichotillomania

Reference	Main results
Fornes-Romero <sup>18</sup>	In OCD patients, “just-right” experiences correlated with severity of compulsions and were associated with ordering, washing, or hoarding symptoms.
Hirschtritt <sup>19</sup>	Aggressive urges were linked to TS, OCD, and ADHD.
Subira <sup>20</sup>	67% of 106 OCD patients presented sensory phenomena.
Kano <sup>21</sup>	Level of sensory phenomena and urges correlated with YGTSS and DY-BOCS. Sensory phenomena correlated with OCD aggression and sexual/religious dimensions.
Gillan <sup>22</sup>	In 25 OCD patients, habits were associated with urges.
Brandt <sup>23</sup>	In OCD patients, urges presented an inverted U evolution around compulsions.
Rachman <sup>24</sup>	In OCD patients, execution of rituals was associated with marked anxiety or urges.
Likierman <sup>25</sup>	Compulsive urges improve spontaneously with time.
Prado <sup>26</sup>	Sensory phenomena were associated with tic-related OCD subtypes and were particularly present in early-onset OCD.
Shavitt <sup>27</sup>	OCD patients with tic disorder were more likely than OCD patients without tic disorder to have urges and sensory phenomena.
Miguel <sup>28</sup>	Urges and sensory phenomena were more frequent in TS patients and TS + OCD patients than in OCD-only patients. “Just-right” experiences were more frequent in OCD + TS patients than in OCD-only or TS-only patients.

Continued on next page

**Table 1** (*continued*)

Reference	Main results
McGuire <sup>29</sup>	Patients with tic disorders presented an average of three different urges.
Brandt <sup>30</sup>	Level of urge intensity was more important when TS patients tried to suppress their tic. The intensity decreased after the tics.
Schunke <sup>31</sup>	There was no correlation between urge intensity and sensory perceptions in TS patients.
Brabson <sup>32</sup>	The relationship between tics and urges was difficult to interpret in this study of TS patients.
McGuire <sup>33</sup>	Urge presence at baseline was associated with remission after behavioral intervention in TS patients.
Ganos <sup>34</sup>	The higher the urge intensity, the later TS patients were conscious of their voluntary action.
Muller-Vahl <sup>35</sup>	Urge intensity was not changed by tic suppression in TS patients. There was no correlation between tic severity and level of urges.
Capriotti <sup>36</sup>	Urges were more intense during tic suppression than at baseline in TS patients.
Cohen <sup>37</sup>	82% of TS patients presented urges; 57% of these patients with urges found that urges were more bothersome than tics.
Sambrani <sup>38</sup>	In TS patients, tic severity was associated with level of urges. Urges were highly associated with “just-right” experiences.
Eapen <sup>39</sup>	TS patients with complex tics reported more urges than TS patients with simple tics.
Ganos <sup>40</sup>	The more TS patients had interoceptive awareness, the more they had urges. Tic severity was associated with urge intensity.
Reese <sup>41</sup>	Level of urges correlated with tic severity, but not with severity of comorbid OCD in TS patients.
Eddy <sup>42</sup>	“Non-obscene socially inappropriate symptoms” were associated with more urges in TS patients.
Crossley <sup>43</sup>	Urges were associated with vocal tic severity and compulsivity in TS patients.
Rajagopal <sup>44</sup>	Different types of urges are associated with tics and compulsive symptoms in TS patients.
Gulisano <sup>45</sup>	No correlation between urge intensity and tic severity, but correlation found between urge intensity and compulsive symptoms in TS patients.
Steinberg <sup>46</sup>	Urge intensity was not correlated with tic severity, but was correlated with compulsion in TS patients (only in those under age 10, however).
Lee <sup>47</sup>	Acceptance and commitment therapy did not improve urges in TTM patients.
Falkenstein <sup>48</sup>	In TTM patients, TTM-by-proxy urges were present in 54% of the sample.

ADHD = attention deficit/hyperactivity disorder; DY-BOCS = Dimensional Yale-Brown Obsessive-Compulsive Scale; OCD = obsessive-compulsive disorder; TS = Tourette syndrome; TTM = trichotillomania; Y-BOCS = Yale-Brown Obsessive-Compulsive Scale; YGTSS = Yale Global Tic Severity Scale.

washing or checking compulsions classically associated with anxiety) that have been more frequently associated with tics than with compulsions.<sup>9</sup> What highlights the difficulty of determining whether urges are associated with OCD, TS, or both is that some studies found a correlation between level of urges as measured by the Premonitory Urge to Tic Scale (PUTS) and the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS), but not between PUTS and the Yale Global Tic Severity Scale (YGTSS),<sup>45,46</sup> whereas other studies found the opposite.<sup>40,41</sup> Unfortunately, among these studies,<sup>40,41,45,46</sup> none made specific correlations between PUTS scores and different types of OCD to determine whether PUTS scores were associated with specific compulsions (e.g., symmetry) or with symmetry and checking compulsions alike. However, when considering studies which made the distinction between different types of “compulsions,”<sup>20,21,38,41,44</sup> urges were associated with symmetry compulsions or “just-right”

perception, phenomena more frequently associated elsewhere with TS than with OCD,<sup>9</sup> and never specifically with repetitive checking or washing behaviors, which are more frequently associated with OCD.<sup>9</sup>

As in Tourette and OCD, urges are found in TTM.<sup>47</sup> The urge to pull was greater in patients who experienced perfectionistic thoughts,<sup>48</sup> which could be associated with symmetry or “just-right” phenomena.

Taken together, even if it is impossible to reach a definitive conclusion, it seems that urges are specifically associated with specific repetitive behaviors: tics, symmetry, or “just-right” phenomena. Furthermore, in TTM, urges are associated with perfectionistic thoughts, which could be considered as being close to the “just-right” phenomenon. These phenomenological descriptions could suggest an important overlap between TTM and tic disorders, maybe more so than with OCD – neither TTM nor tics being preceded by thoughts or images, unlike in OCD.<sup>1</sup> Furthermore, one could hypothesize that urges in OCD

would in fact precede complex tics, not compulsions, since it has been shown that compulsions can in some cases be considered tics.<sup>9</sup>

Finally, a very important study on the phenomenology of TTM<sup>49</sup> found significant differences between TTM and OCD, but not between TTM and tic disorders (chronic tic disorder and TS), particularly when multiple symptoms were taken into consideration, such as anxiety symptoms (as measured by the Multidimensional Anxiety Scale for Children [MASC]), depressive symptoms (as measured by the Children's Depression Inventory [CDI]), internalizing symptoms, externalizing symptoms, and thoughts (as measured by the Child Behavior Checklist [CBCL]). This study<sup>49</sup> thus found a more important relationship between tic disorders and TTM when co-symptoms of TTM, OCD, and tic disorders were considered, as our qualitative comparison of DSM-5 diagnostic criteria did.

### Comorbidity

Comorbidity results are presented in Table 2.

Comorbidity rates among TS, OCD, and tic disorder

OCD and TTM are frequently comorbid. The studies included in this review reported a 6 to 11% rate of TTM

**Table 2** Epidemiological data in obsessive-compulsive disorder, Tourette syndrome, and trichotillomania

Reference	Main results
Torresan <sup>5</sup>	OCD patients: 6.9% had comorbid TTM 8.4% had comorbid TS 28.2% had comorbid tic disorders
Bienvenu <sup>6</sup>	OCD patients: 11% had comorbid TTM 18% had comorbid tic disorders
Hemmings <sup>7</sup>	Early-onset OCD: 19% had comorbid tic disorders 7.5% had comorbid TS 5.8% had comorbid TTM Late-onset OCD: 9.3% had comorbid tic disorders 1% had comorbid TS 0.88% had comorbid TTM
Richter <sup>8</sup>	OCD patients: 9% had comorbid TTM 13% had comorbid tic disorders
Lochner <sup>10</sup>	OCD patients: 12.3% had comorbid tic disorders 3.8% had comorbid TS TTM patients: 6.1% had comorbid tic disorders 2% had comorbid TS
Stewart <sup>50</sup>	18.8% of OCD patients had comorbid TTM
Brakoulias <sup>51</sup>	11.5% of OCD patients had comorbid TTM
Lochner <sup>52</sup>	OCD patients: 6.4% had comorbid TTM

**Table 2** (continued)

Reference	Main results
	13.1% had comorbid tic disorders 4.80% had comorbid TS
Bienvenu <sup>53</sup> Jaisooriya <sup>54</sup>	4% of OCD patients had comorbid TTM 8% of patients with OCD + tic disorders had comorbid TTM 0.7% of patients with OCD without tic disorders had comorbid TTM
Lovato <sup>55</sup>	26.7% of patients with pure OCD had comorbid tic disorders 33.1% of patients with OCD + grooming disorders had comorbid tic disorders
Robertson <sup>56</sup>	40-60% of TS patients had comorbid OCD
Greenberg <sup>57</sup>	53% of TS patients had comorbid OCD
Frank <sup>58</sup>	TS patients: 13.8% had comorbid OCD 9.7% had comorbid TTM
Houghton <sup>59</sup> Greenberg <sup>60</sup>	7.1% of TTM patients had comorbid OCD TTM patients: 18.1% had comorbid OCD 2.9% had comorbid tic disorders
Grant <sup>61</sup>	TTM patients: 10-15% had a family history of TTM 3.1-18.4% had a family history of OCD
Odlaug <sup>62</sup>	8.3% of TTM patients had comorbid OCD
Panza KE <sup>63</sup>	TTM patients: 5% had comorbid OCD 6% had comorbid tic disorders
King <sup>64</sup>	TTM patients: 2 of 15 had comorbid OCD 2 of 15 had comorbid tic disorders
Hanna <sup>65</sup>	9% of patients with TTM had comorbid tic disorders 0% of patients with OCD had comorbid tic disorders
Keuthen <sup>66</sup>	TTM patients: 38% had comorbid OCD 2.7% had comorbid TS
Hirschtritt <sup>67</sup>	66% of patients with TS had comorbid obsessive-compulsive spectrum disorders

OCD = obsessive-compulsive disorder; TS = Tourette syndrome; TTM = trichotillomania.

comorbidity in patients with OCD.<sup>5-8,50-53</sup> However, we found also that OCD patients with TTM have more tics than those without TTM<sup>50</sup>; and OCD patients with TTM have an earlier onset of their OCD.<sup>50</sup> The same results have been found for OCD patients with tics: they are more likely to have comorbid TTM than OCD patients without tics<sup>54</sup> and have an earlier age of OCD onset.<sup>54</sup>

When considering OCD patients with and without "grooming disorders," we found that the two groups presented the same frequency of tic disorder; however, OCD patients without grooming disorders more often had

a family history of tics, while OCD patients with grooming disorder more often had a family history of OCD.<sup>55</sup>

Finally, patients with early-onset OCD have more TS/tics and TTM comorbidity than those with late-onset OCD.<sup>7,56</sup> These data are important from a genetic standpoint (see Genetics section below).

An interesting study looked at the family history of OCD patients and found that 55% of their family members had a history of OCD, 14% had a history of tic disorders, and only 4% had a history of TTM.<sup>6</sup> The authors concluded that “it seems reasonable to consider TTM OCD-related,” but also that “OCD and tic disorders are strongly family-related, and from this standpoint, it would be sensible to group these conditions together in DSM-5.”<sup>6</sup>

When we searched for studies on comorbid TTM in TS patients, we found that about 3.8-10% of TS patients also have TTM.<sup>57,58</sup> More importantly, in a multivariable analysis of TTM occurring in TS patients, one of these studies found that only Yale-Global Tic Severity Scale (YGTSS) motor score was associated with occurrence of TTM in comorbidity with TS.<sup>57</sup> In this same multivariable analysis, comorbid OCD was not associated with occurrence of TTM in TS patients.<sup>57</sup>

Finally, we found that between 2.6 and 20% of TTM patients had a history of OCD,<sup>49,53,59-62</sup> while 0 to 3% had a history of tic disorders.<sup>53,60</sup>

When comparing tic comorbidity in OCD and TTM patients, five studies reported that TTM patients have the same level of tic disorders as OCD patients.<sup>10,49,63-65</sup> However, another study found distinct results, with TTM patients having much more OCD than tic disorders.<sup>66</sup> If we consider TTM as a tic, the rate of OCD comorbidity in TTM in this latter study is then close to the one found in TS.<sup>67</sup>

These studies highlight a relationship between tics and TTM, not only in an OCD context (and, possibly, in the specific context of early-onset OCD<sup>7,54</sup>), but also directly in TS patients.<sup>57</sup> This last study helps us reach the conclusion that the TTM-tic relationship seems stronger than the TTM-OCD relationship, since OCD was not associated with occurrence of TTM in TS patients.

#### Comorbidity rates of TTM, OCD, and tic disorder with other psychiatric disorders

When we looked at other comorbidities in each of these disorders, we found that: 1) TTM patients have a lifetime rate of comorbid major depressive disorder (MDD) of approximately 43%<sup>59</sup>; 2) OCD patients present have a 15 to 55% lifetime rate of comorbid MDD<sup>68-70</sup>; and 3) TS patients have a 13 to 76% lifetime rate of comorbid MDD.<sup>56,67</sup>

Hence, there are major discrepancies between studies of depressive comorbidity (e.g., some studies reported a 15% rate of comorbid MDD in TS, whereas another reported 60%<sup>56</sup>). It is thus very difficult to reach any conclusions. Concerning other psychiatric comorbidities in TTM, OCD, and tic disorders, results also preclude any conclusions.<sup>59,67-74</sup> Furthermore, comorbidity studies in patients with OCD or TS are much easier to find than in TTM patients.

#### Comparison of TTM, OCD, and tic disorder epidemiology

Epidemiological data favor a closer proximity between TTM and OCD than between TTM and tic disorders. Just as OCD (about 55% of patients are female), TTM affects more women than men (about 80-85% of patients are female); this is not the case in TS, which affects males more often females.<sup>49,75-81</sup> Nonetheless, some studies found a greater proportion of males in OCD.<sup>82</sup> Age of onset in TTM (about 11 to 13 years) is approximately the same as for early-onset OCD (about 11 years), but onset of tic disorders occurs much earlier (about 4 to 8 years).<sup>1,75,80,81,83-86</sup> On a developmental level, analysis of the age at onset and the course of these illnesses seems to show TTM is closer to OCD (both chronic disorders) than to tic disorders (in which nearly half of patients become tic-free in early adulthood).<sup>75,81,83,87-89</sup> Conversely, however, we could highlight that tic disorders tend to worsen in early adolescence (10-12 years),<sup>1</sup> when OCD and TTM appear.

Hence, even if lifetime prevalences are nearly similar across these disorders (about 1 to 3% for TTM,<sup>1,75,83</sup> about 2% for OCD,<sup>90</sup> and about 1% for TS<sup>80,91</sup>), epidemiological data seem to favor a closer relationship between TTM and OCD than between TTM and tic disorders.

#### Neuropsychology

Another way to study the proximity between OCD, tic disorders, and TTM is to analyze the neuropsychological particularities of each of these disorders (Table 3).

First, when comparing these three disorders, we find that adults with OCD<sup>12</sup> seem to show a motor inhibition deficit, but no such deficit was found in children.<sup>13</sup> Results in TTM are divergent; some authors found an inhibition deficit (Stop Signal task, Go-No Go Test<sup>92-95</sup>), while others did not (Stop Signal task,<sup>95,96</sup> Go-No Go Test<sup>94</sup>). Authors found no deficit for the Go-No Go or Stop Signal tasks in TS.<sup>14</sup> It is thus difficult to compare these three disorders in terms of inhibition, because of the divergent findings in TTM. Second, altered flexibility was found in adults with OCD<sup>12</sup> (but not in children<sup>13</sup>) and in TS,<sup>15</sup> but not in TTM<sup>93,95,97-99</sup> (except in one study, which found a deficit in the Object Alternation task, but not in the Wisconsin Card Sorting Test [WCST]<sup>100</sup>). Attention deficits are found in all three disorders,<sup>12,101</sup> but more mixed results are found in TS (some studies found a deficit,<sup>102-104</sup> whereas others did not<sup>105-107</sup>). However, one must keep in mind that attention deficit/hyperactivity disorder (ADHD) is a frequent comorbidity in TS and that the attention deficit results mentioned above seem linked only to comorbid ADHD. Finally, concerning working memory, adult OCD patients presented deficits,<sup>12</sup> but children did not.<sup>13</sup> In TTM, no difference from controls was found.<sup>97,100,108</sup> In TS patients, some studies reported deficits<sup>106,109-113</sup> while others did not.<sup>114</sup>

Looking at these data, TTM seems closer to TS than to OCD. However, bearing in mind the many divergent findings in these neuropsychological studies and that very few have been conducted in TTM, no definitive conclusion

**Table 3** Neuropsychological data in obsessive-compulsive disorder, Tourette syndrome, and trichotillomania

Reference	Main results
Abramovitch <sup>12</sup>	In adults with OCD Attention deficit Working memory deficit Flexibility deficit Inhibition deficit
Abramovitch <sup>13</sup>	In children with OCD No working memory deficit No flexibility deficit No inhibition deficit
Morand-Beaulieu <sup>14</sup>	Inhibition deficit in TS patients
Lange <sup>15</sup>	Cognitive flexibility deficit in TS patients
Odlaug <sup>92</sup>	Inhibition deficit in TTM patients
Chamberlain <sup>93</sup>	Inhibition deficit in both TTM and OCD patients
Bohne <sup>94</sup>	Greater inhibition deficit in younger TTM patients than in older TTM patients. The deficit was greater than in OCD patients.
Grant <sup>95</sup>	Inhibition deficit in TTM patients in the stop-signal reaction test
Brennan <sup>96</sup>	Better inhibition performance than healthy controls in TTM patients
Flessner <sup>97</sup>	No flexibility deficit No working memory deficit
Chamberlain <sup>98</sup>	Working memory deficit in OCD patients and in TTM patients No difference in working memory between OCD and TTM patients No flexibility deficit in TTM patients, but flexibility in OCD patients
Grant <sup>99</sup>	No flexibility deficit in TTM patients
Bohne <sup>100</sup>	No difference in working memory between TTM patients, OCD patients, and healthy controls Flexibility deficit in TTM patients Flexibility deficit in OCD patients
Stanley <sup>101</sup>	Divided attention deficit in TTM patients
Termine <sup>102</sup>	Inhibition deficit in TS patients Attention deficit in TS patients
Sukhodolsky <sup>103</sup>	No inhibition deficit in TS patients without ADHD Attention deficit in TS patient with ADHD
Shucard <sup>104</sup>	Attention deficit in TS patients
Matsuda <sup>105</sup>	Flexibility deficit in TS patient with aggressive obsessions
Chang <sup>106</sup>	Attention and working memory deficits in TS and OCD patients
Sherman <sup>107</sup>	No attention deficit in TS-only patients
Keuthen <sup>108</sup>	No attention or working memory deficit in TTM patients
Jeter <sup>109</sup>	Working memory and inhibition deficit in TS patients

**Table 3** (continued)

Reference	Main results
Eddy <sup>110</sup>	Working memory and inhibition deficit in TS patients
Crawford <sup>111</sup>	No working memory deficit in TS patients
Channon <sup>112</sup>	No working memory deficit in TS patients
Bornstein <sup>113</sup>	No working memory deficit in TS patients
Channon <sup>114</sup>	No working memory deficit in TS patients

OCD = obsessive-compulsive disorder; TS = Tourette syndrome; TTM = trichotillomania.

can be drawn as to a close relationship between TTM and either OCD or TS.

Some authors have directly compared OCD and TTM and found that TTM patients have less flexibility dysfunction than OCD patients, as well as a greater impulse control deficiency,<sup>93,115</sup> although the latter is less clear.<sup>94</sup> Studies based on other neuropsychological tasks, such as response monitoring<sup>116</sup> and strategy implementation,<sup>117</sup> also reached the conclusion that there are differences between OCD and TTM. Direct neurocognitive comparisons between TTM and TS are much harder to find.

In conclusion, from a neurocognitive point of view, TTM seems closer to TS than to OCD, but the many limitations in such research preclude any definitive conclusion.

## Neurobiological comparison between TTM, OCD, and tic disorders

### Imaging studies

When TTM, TS, and OCD imaging studies<sup>16,17,92,118-136</sup> were compared (Table 4), striatal abnormalities were found in the three disorders. No other common abnormality is found in OCD and TTM (Table 4). In imaging studies of TS and TTM,<sup>122,129</sup> increased precentral gyrus volume has been reported in both disorders (since the supplementary motor area [SMA] is part of the precentral gyrus), not in OCD (Table 4).<sup>16,17</sup>

There is evidence that the SMA is involved in the neurobiology of tics<sup>137</sup>; hence, the finding of SMA abnormalities in both TS and TTM imaging studies could suggest a neurobiological relationship between TTM and TS. Unfortunately, it is difficult to reach any definitive conclusion, as meta-analyses of VBM studies in TTM and TS are still lacking; nonetheless, the current data seem to favor a closer relationship between TTM and TS than between TTM and OCD.

Concerning diffusion tensor imaging (DTI) studies, we found only one study in TTM,<sup>138</sup> which hinders comparisons with DTI meta-analyses in OCD or with the several DTI studies in TS. The same applies to functional connectivity studies (we found only one<sup>139</sup> in TTM) and functional MRI in TTM (where we found only three studies on different specific tasks<sup>139-141</sup>).



**Table 4** Neuroimaging data in obsessive-compulsive disorder, Tourette syndrome, and trichotillomania vs. healthy controls

Reference	Main results
Odlaug <sup>92</sup>	In TTM patients Increased right inferior/middle frontal cortical thickness Increased right lingual cortical thickness
Roos <sup>118</sup>	In TTM patients Decreased right parahippocampal cortical thickness
Keuthen <sup>119</sup>	In TTM patients Decreased cerebellum volume
O'Sullivan <sup>120</sup>	In TTM patients Decreased left putamen volume
Grachev <sup>121</sup>	In TTM patients Decreased left inferior frontal gyrus volume Increased right cuneal cortex volume
Chamberlain <sup>122</sup>	In TTM patients Increased left striatum grey matter density Increased left amygdalo-hippocampal formation grey-matter density Increased cingulate cortex grey-matter density Increased supplementary motor cortex grey-matter density
Hu <sup>16</sup>	In OCD patients Increased striatal volume Decreased prefrontal cortex volume Decreased left visual cortex volume (in children) Decreased anterior cingulate cortex volume (in adults) Decreased cerebellum volume (in adults)
Boedhoe <sup>17</sup>	In OCD patients Decreased hippocampal volume Increased pallidum volume Increased thalamic volume (in children)
Peterson <sup>123</sup>	In TS patients Decreased left lenticular nucleus volume
Peterson <sup>124</sup>	In TS patients Decreased caudate volume Decreased lenticular nucleus volume
Lee <sup>125</sup>	In TS patients Increased left thalamus volume
Ludolph <sup>126</sup>	In TS patients Increased ventral putamen volume Decreased left hippocampal gyrus grey-matter volume
Draganski <sup>127</sup>	In TS patients Decreased orbitofrontal cortex grey-matter volume Decreased anterior cingulate cortex grey-matter volume Decreased ventrolateral prefrontal cortex grey-matter volume
Wittfoth <sup>128</sup>	In TS patients Decreased left inferior frontal gyrus grey-matter volume
Liu <sup>129</sup>	In TS patients Decreased left superior temporal gyrus grey-matter volume Increased left paracentral gyrus grey-matter

**Table 4** (continued)

Reference	Main results
	volume Increased right precentral gyrus grey-matter volume Decreased right precentral cortex white-matter volume Decreased right precuneus cortex white-matter volume Decreased left temporal occipital fusiform cortex white-matter volume Decreased right frontal pole white-matter volume Decreased right postcentral gyrus white-matter volume Decreased lingual gyrus white-matter volume Decreased orbitofrontal cortex white-matter volume
Greene <sup>130</sup>	In TS patients Decreased medial prefrontal cortex white-matter volume Increased posterior thalamus grey-matter volume Increased hypothalamus grey-matter volume Increased midbrain grey-matter volume
Forde <sup>131</sup>	In TS patients No modification of basal ganglia volumes
Roessner <sup>132</sup>	In TS patients No brain alteration
Muller-Vahl <sup>133</sup>	In TS patients Decreased gray-matter volume in: - Left postcentral gyrus - Right cingulate gyrus - Left caudate - Left middle frontal gyrus - Left precentral gyrus - Right middle frontal gyrus - Right precentral gyrus - Right postcentral gyrus - Right medial frontal gyrus - Left cingulate gyrus Decreased white-matter volume in: - Right inferior frontal gyrus - Left superior frontal gyrus - Left precentral gyrus - Right anterior corpus callosum - Left lingual gyrus Increased white-matter volume in: - Left postcentral gyrus - Left precentral gyrus - Left precentral gyrus - Right parahippocampal gyrus - Right precentral gyrus
Isobe <sup>134</sup>	In TTM patients Decreased right amygdala Decreased left putamen
Chamberlain <sup>135</sup>	In TTM patients Increased right inferior frontal gyrus cortical thickness No difference for subcortical structures
Stein <sup>136</sup>	No differences concerning ventricular/brain ratio and caudate volume between OCD and TTM patients and healthy controls

OCD = obsessive-compulsive disorder; TS = Tourette syndrome; TTM = trichotillomania.

## Genetic studies

### Heritability

Comparing heritability could be a good way to disentangle the TTM-OCD-TS relationship. Heritability in OCD was reported as 40-50% in studies conducted in the 2000s,<sup>142</sup> compared to 32-76% in TTM<sup>142</sup> and 25-77% in TS.<sup>143</sup> Given the huge differences in heritability across different studies, no conclusion can be reached concerning the relationship of TTM with either OCD or TS in this respect.

### Candidate gene studies

Genetic studies – and, more specifically, candidate gene studies – could be useful to compare the neurobiology of TTM, TS, and OCD. Altered genes shared between two of these disorders could suggest that common intracellular pathways are involved.

One study found that a variant of *SAPAP3* was associated with TTM, but this result did not withstand correction for multiple comparisons.<sup>144</sup> The same study also found that a specific haplotype of *SAPAP3* was linked with earlier onset of OCD, but no difference in genotype or allele frequencies for *SAPAP3* was found for OCD compared to controls.<sup>144</sup> Furthermore, this study did not mention the nature of compulsions, which would have been useful, knowing that tic disorders begin earlier than OCD and that some compulsions are strongly associated with tic disorders (e.g., symmetry compulsions, as noted in the Phenomenology section). Another study found an association between a *SAPAP3* variant and TTM, but no association was found between *SAPAP3* variants and OCD.<sup>145</sup> A third study found that two specific variants of *SAPAP3* and two specific haplotypes could be linked with TS, but the results were no longer significant after correction.<sup>146</sup> Hence, the *SAPAP3* gene may be linked directly to TS and TTM, but only with the age of onset in OCD.

Another study found that the T102T genotype for *5HTR2A* was more frequent in TTM patients than in controls (result remained significant after correction) and OCD patients (result did not remain after correction).<sup>147</sup> Thus, one might think that *5HTR2A* polymorphisms are specific to TTM, but a meta-analysis of genetic association studies in OCD found that *5HTR2A* polymorphisms were in fact also associated with OCD.<sup>148</sup> Finally, a recent study found no association between *5HTR2A* polymorphisms and TS.<sup>149</sup> Thus, considering *5HTR2A* polymorphisms, one might presume that TTM is closer to OCD than TS.

*SLITRK1* variants are associated with OCD,<sup>150,151</sup> but also with TTM and TS.<sup>90,151-154</sup> This gene seems involved in vulnerability for all three of these disorders.

We did not find any study on links between other candidate genes known to be possibly involved in OCD neurobiology<sup>90,148</sup> and TTM. However, some studies on these genes included patients with both TS and OCD.<sup>155,156</sup> Likewise, we did not find any studies on links between TS candidate genes not mentioned above<sup>153,154,157,158</sup> and TTM. Among these studies, some included patients with both TS and OCD.<sup>158-160</sup>

It is difficult to draw any conclusion from these studies. *SAPAP3* appears to be somehow associated with TS and TTM, *5HTR2A* with OCD and TTM, and *SLITRK1* with all three disorders. Thus, nothing can be presumed about a relationship between these disorders from a candidate gene standpoint. Furthermore, some of the genes potentially involved in these disorders and mentioned above have also been implicated in schizophrenia<sup>161</sup> and autism.<sup>162</sup> The only conclusion we can reach is already well known: OCD, TS, and TTM seem to be genetically related disorders.

### Cluster analysis

In terms of genetics, OCD and TS have been considered to be on the same spectrum and genetically linked.<sup>163,164</sup> More recently, a significant genetic correlation has been found between these two disorders, similar to the genetic correlation between bipolar disorder and MDD.<sup>165</sup> Different studies that looked at the relationships between TS and OCD in terms of phenotypes found different, complex relationships, which could lead to different TS or OCD subclasses.<sup>10,166-169</sup> When we analyzed the place of TTM in these different subclasses of OCD or TS, we found only studies on OCD. First, a three-cluster OCD model placed TTM and TS were in the same cluster (called “reward deficiency”)<sup>170</sup>; second, in a three-subclass OCD model, OCD with tics was more often associated with grooming disorders, which included TTM and pathological skin picking.<sup>169</sup> From the standpoint of these studies, if TTM can be associated with any OCD subclass, it seems that in these cases TTM is also associated with tic disorders. These results may shed light on a potential relationship between tic disorders and TTM in the global context of OCD.

Finally, a key study on latent liability factor found two factors, with the first factor common to all obsessive-compulsive related disorders (but with the strongest loading for OCD, body dysmorphic disorder, and hoarding disorder) and a second factor loaded only by TTM and skin-picking disorder.<sup>171</sup> Hence, this study highlights the relative distance (essentially genetic) between OCD and TTM.

## Treatment

Another potentially relevant approach to distinguishing the tic or OCD nature of TTM is to compare the efficacy of different treatment types in OCD, tic disorder, and TTM (Table 5). It should be noted that not all treatments mentioned below are approved by the U.S. Food and Drug Administration (FDA) for treating the different disorders studied.

When we look at these different data, treatment of TTM appears to resemble that of TS treatment, with antipsychotics<sup>172-195</sup> seemingly effective and selective serotonin reuptake inhibitors (SSRI)<sup>196-202</sup> ineffective (while SSRIs are a well-established treatment for OCD<sup>203-214</sup>). A meta-analysis found serotonin reuptake inhibitors (SRI) to be effective in TTM,<sup>215</sup> contradicting a previous meta-analysis.<sup>198</sup> This difference may be explained by study

**Table 5** Studies of pharmacotherapy in obsessive-compulsive disorder, Tourette syndrome, and trichotillomania

Reference	Main results
Hollis <sup>172</sup>	Antipsychotics are effective in reducing tics in TS patients (meta-analysis)
Zheng <sup>173</sup>	Aripiprazole as effective as haloperidol or tiapride in reducing tics in TS patients (meta-analysis)
Van Ameringen <sup>174</sup>	Olanzapine as an effective treatment in TTM
Howard <sup>175</sup>	Aripiprazole as an effective treatment of TTM in a patient suffering from Huntington disease (case report)
Yasui-Furukori <sup>176</sup>	Aripiprazole as an effective treatment of TTM (case report)
White <sup>177</sup>	Aripiprazole as an effective treatment of TTM
Virit <sup>178</sup>	Aripiprazole as an effective treatment of TTM (case report)
Jefferys <sup>179</sup>	Aripiprazole as an effective treatment of TTM (case report)
Van Ameringen <sup>180</sup> Crescente Jr. <sup>181</sup> Khouzam <sup>182</sup>	Haloperidol as an effective treatment of TTM (in nine patients, no control group) Efficacy of quetiapine in TTM (case report) Efficacy of quetiapine in TTM (case report)
Stewart <sup>183</sup>	Olanzapine as an effective treatment in TTM
Liu <sup>184</sup>	Aripiprazole as an effective treatment in TS (meta-analysis)
Oravec <sup>185</sup>	Risperidone as an effective treatment of TTM (case report)
Mancini <sup>186</sup>	Antipsychotics as an effective treatment in TTM (case series)
Ashton <sup>187</sup>	Olanzapine as an effective treatment in TTM (four cases)
Senturk <sup>188</sup>	Risperidone as an effective treatment of TTM (case report)
Srivastava <sup>189</sup>	Olanzapine as an effective treatment of TTM (two cases)
Potenza <sup>190</sup>	Olanzapine as an effective treatment in TTM (case report)
Epperson <sup>191</sup>	Risperidone as an effective treatment of TTM (three cases)
Gabriel <sup>192</sup>	Risperidone as an effective treatment of TTM (case report)
Ghaziuddin <sup>193</sup>	Haloperidol as an effective treatment of TTM (case report)
Stein <sup>194</sup>	Pimozide as an effective treatment of TTM (in six cases out of seven)
Pathak <sup>195</sup>	Olanzapine as an effective treatment of TTM (case report)

**Table 5** (continued)

Reference	Main results
Rothbart <sup>196</sup>	No efficacy of SSRI in TTM (Cochrane review)
Rothbart <sup>197</sup>	No efficacy of SSRI in TTM (Cochrane review)
Bloch <sup>198</sup>	No efficacy of SSRI but efficacy of clomipramine in TTM (meta-analysis)
Christenson <sup>199</sup>	No efficacy of fluoxetine in TTM
Streichenwein <sup>200</sup>	No efficacy of fluoxetine in TTM
Van Minnen <sup>201</sup>	No efficacy of fluoxetine in TTM
Scahill <sup>202</sup>	No efficacy of fluoxetine in TS
Issari <sup>203</sup>	Efficacy of SSRI in OCD (meta-analysis)
Romanelli <sup>204</sup>	Efficacy of SRI in OCD (meta-analysis)
Bloch <sup>205</sup> Soomro <sup>206</sup>	Efficacy of SSRI in OCD (meta-analysis) Efficacy of SSRI in OCD (meta-analysis)
Ivarsson <sup>207</sup>	Efficacy of SRI in OCD (meta-analysis)
McGuire <sup>208</sup>	Efficacy of SRI in OCD (meta-analysis)
Stein <sup>209</sup>	Efficacy of SRI in OCD (meta-analysis)
Sanchez-Meca <sup>210</sup>	Efficacy of SRI in OCD (meta-analysis)
Geller <sup>212</sup>	Efficacy of SSRI in OCD (meta-analysis)
Piccinelli <sup>213</sup>	Efficacy of SRI in OCD (meta-analysis)
Varigonda <sup>214</sup>	Efficacy of SSRI in OCD (meta-analysis)
McGuire <sup>215</sup>	Efficacy of SRI in TTM (meta-analysis)
Caine <sup>216</sup> Bloch <sup>217</sup>	No efficacy of SRI TS Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Veale <sup>218</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Dold <sup>219</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Dold <sup>220</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Skapinakis <sup>221</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Maher AR <sup>222</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)
Fineberg <sup>223</sup>	Efficacy of antipsychotics in OCD as an augmentation treatment (meta-analysis)

OCD = obsessive-compulsive disorder; SRI = serotonin reuptake inhibitor; SSRI = selective SRI; TS = Tourette syndrome; TTM = trichotillomania.

selection: two clomipramine studies were included in the meta-analysis by McGuire,<sup>215</sup> but not in Bloch's,<sup>198</sup> which was limited to SSRI studies. Indeed, clomipramine seems to have a place in the treatment of both TTM and

OCD,<sup>198,214</sup> which is not the case for TS.<sup>216,224</sup> Furthermore, antipsychotics also seem to have a place in treatment strategies for OCD<sup>217-223</sup> to augment SSRI efficacy. However, this raises diagnostic questions. The fact that some compulsions can be easily confused with tics could explain the efficacy of adjunctive antipsychotic treatment in OCD.<sup>9</sup> Finally, *N*-acetylcysteine has been debated for treatment of these conditions, with mixed results across different studies.<sup>196,225-231</sup>

The efficacy of other treatments used in TS or OCD could not be examined in TTM due to a lack of data. For example, clonidine, which is effective in TS,<sup>232</sup> has not been studied in TTM; amantadine<sup>233</sup> and memantine,<sup>234</sup> which have shown adjunctive efficacy in treatment-refractory OCD, have not been studied in TTM to the best of our knowledge. Finally, deep brain stimulation, which has been found highly effective in OCD<sup>235</sup> and TS,<sup>236,237</sup> has not been studied in TTM (although a complex case of Parkinson's disease with comorbid TTM treated by deep brain stimulation has been reported<sup>238</sup>).

Concerning psychotherapies, habit reversal training has shown efficacy in TTM<sup>198,239-245</sup> and TS,<sup>243,245-248</sup> while exposure response prevention (ERP) seems to be the most efficient psychotherapy for OCD.<sup>243,249,250</sup>

## Discussion

TTM is widely and rightly accepted as a part of the OCD spectrum, based in part on its repetitive phenomenology.<sup>1</sup> However, difficulties in distinguishing OCD and TS in some cases<sup>9</sup> led us to the question of whether the real nature of TTM is indeed obsessive-compulsive rather than tic-related. We thus examined the literature on TTM, OCD, and tic disorders. We divided this literature review into five different axes (phenomenology, epidemiology, neuropsychology, neurobiology, and treatment), to provide clearer insight into the true nature of TTM.

This review allowed us to go beyond the classical question of "is TTM related to OCD?"<sup>251</sup> and ask: "is TTM related to tic disorders?" If data from candidate gene studies does not provide clear answers, other information can help. Epidemiological data showed different results concerning age of onset and course of these disorders, but suggesting a closer link between TTM and OCD, while studies of comorbidity (especially rates of TTM, OCD, and TS comorbidity among these conditions) seemed to suggest a closer link between TTM and TS.<sup>57</sup> It is difficult to reach a conclusion according to these epidemiological data.

Conversely, clinical, imaging, neuropsychological, cluster-analysis, and, most importantly, treatment studies lead us to think that there is a closer relationship between TTM and tic disorders.

Imaging studies have implicated motor regions, especially the supplementary motor area, in TTM and tic disorders,<sup>122,129</sup> but not in OCD.<sup>16,17</sup> Even if these findings lack confirmation from meta-analyses, they highlight the motor characteristics of TTM and tic disorders. These aspects are in line with what is seen in clinical practice. OCD patients seem to experience more anxiety than tic-disorder and TTM patients do.<sup>49</sup> Urges are

found in all three disorders; however, in OCD, they seem to pertain more specifically to symmetry or "just-right" compulsions – behaviors that have been associated more frequently with TS than with OCD.<sup>9</sup> Genetic data, especially from cluster-analysis studies (clusters in which genetic backgrounds are supposed to have a major role), endorse relationships between tics and TTM, since both are found in the same clusters.<sup>169-171</sup> Limiting these findings is the fact that these clusters are generated in an OCD context (i.e., from OCD patients), except for one study on latent liability factor which clearly differentiated OCD and TTM.<sup>171</sup> Results from neuropsychological studies are very divergent depending on study design, neuropsychological processes assessed, and tasks employed.<sup>252</sup> Finally, the strongest evidence leading us to the conclusion of a closer relationship between TTM and tic disorders than between TTM and OCD comes from therapeutic studies. In both TS and TTM, antipsychotic treatment is essential.<sup>153,172-182,196,197,232,253-259</sup> Furthermore, the efficacy of antipsychotics in TTM and TS has been shown for a wide range of agents.<sup>153,172-182,196,197,232,253-259</sup>

Together, these data support a closer relationship between TTM and TS than between TTS and OCD. However, TTM is not exactly a tic disorder. As stated much earlier, TS and OCD are on the same spectrum.<sup>163,260</sup> The closer relationship of TTM and OCD in terms of some specific epidemiological data, but not in terms of treatment, suggest that TTM is somewhere on a tic-OCD spectrum, as stated by Hollander et al.<sup>260</sup> TTM is neither exactly a tic disorder nor an OCD subtype, which is congruent with Phillips's conclusions that the overlap between TTM and OCD is "partial at best."<sup>11</sup>

Classifications of psychiatric disorders are only partially based on neurobiological data, which makes them inherently imperfect. Nevertheless, classifications are useful to represent symptoms and support treatment decisions. For these reasons, even if TTM seems to differ from tic disorders in some respects, its phenomenology and treatments (with antipsychotics and/or habit reversal training<sup>239,240,248</sup> showing efficacy in TTM) are closer to those of tic disorders than to those of OCD. Thus, we believe it would be more helpful to consider TTM as a tic disorder in clinical practice. Of course, it is still possible that some TTM patients will present with obsessions and anxiety which lead to their hair pulling; each psychiatrist will have to consider specific cases individually.

The potential tic nature of TTM does not exclude a limbic component in this disorder. As in tic disorders, during stressful periods,<sup>153</sup> the intensity of TTM symptoms can increase<sup>74</sup> (particularly in male patients, according to some authors<sup>261</sup>), which highlights the neurobiological relationship between TTM, tics, and OCD. It is well known that cortico-basal ganglia loops are implicated in OCD and TS,<sup>90,153</sup> with participation of the limbic loop in these two disorders,<sup>90,153</sup> but probably with a differential impact of limbic, associative, and motor loops. The same loops seem to be implicated in TTM.<sup>262,263</sup> These data suggest that OCD, tics, and TTM have to be studied together, as differential or common findings could help improve our understanding of these disorders individually.

Furthermore, considering these disorders together could help improve their treatment, particularly in comorbid or complex contexts.

These data could also help develop treatment methods for refractory TTM cases. As in OCD<sup>235,264</sup> and TS,<sup>265</sup> deep brain stimulation could be of great help to some patients. In these disorders, stimulation targets play a key role,<sup>264,265</sup> and choosing the most effective one is essential. Our data suggest that regions of the basal ganglia targeted in TS (thalamus, postero-ventro-lateral globus pallidus internus, anteromedial globus pallidus internus, and anterior limb of the internal capsule/nucleus accumbens<sup>265</sup>) could be appropriate targets, perhaps more so than OCD targets.

This review has several limitations. Key among them are our qualitative method, without meta-analysis of data, and the lack of studies directly comparing the three disorders in the literature. However, our sample was restricted to original studies and meta-analyses (except for the “antipsychotics in TTM” portion of the pharmacology axis, due to the paucity of original research and absence of meta-analyses).

Much work remains before a truly in-depth understanding of these disorders can be achieved, especially TTM; novel approaches could be helpful. All future research based on neurobiological mechanisms possibly underlying these disorders (e.g., genetic, immunologic, DTI, or animal studies) could help disentangle the relationship between them and, particularly, elucidate the differences in cortico-basal ganglia loop involvement.

In conclusion, despite some discrepancies, we consider that TTM is closer to tic disorders than to OCD, which is confirmed by analysis of phenomenology/symptomatology and treatment efficacy. We believe considering it as such in clinical practice can help psychiatrists better understand and treat patients with TTM.

## Disclosure

The authors report no conflicts of interest.

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