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Trichotillomania comorbidity in a sample enriched for familial obsessive-compulsive disorder

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ABSTRACT

Background: This study addresses the strength of associations between trichotillomania (TTM) and other DSM-IV Axis I conditions in a large sample ($n = 2606$) enriched for familial obsessive-compulsive disorder (OCD), to inform TTM classification.
Methods: We identified participants with TTM in the Johns Hopkins OCD Family Study (153 families) and the OCD Collaborative Genetics Study, a six-site genetic linkage study of OCD (487 families). We used logistic regression (with generalized estimating equations) to assess the strength of associations between TTM and other DSM-IV disorders.
Results: TTM had excess comorbidity with a number of conditions from different DSM-IV chapters, including tic disorders, alcohol dependence, mood disorders, anxiety disorders, impulse-control disorders, and bulimia nervosa. However, association strengths (odds ratios) were highest for kleptomania (6.6), pyromania (5.8), OCD (5.6), skin picking disorder (4.4), bulimia nervosa (3.5), and pathological nail biting (3.4).
Conclusions: TTM is comorbid with a number of psychiatric conditions besides OCD, and it is strongly associated with other conditions involving impaired impulse control. Though DSM-5 includes TTM as an OCD-related disorder, its comorbidity pattern also emphasizes the impulsive, appetitive aspects of this condition that may be relevant to classification.

1. Introduction

Trichotillomania (TTM) is an understudied condition that involves chronic, repetitive hair pulling leading to noticeable, unwanted hair loss [1,2]. Prior to DSM-5, TTM was classified as an impulse-control disorder [1]. In DSM-5, the authors re-classified TTM as obsessive-compulsive disorder (OCD)-related, in a new chapter that also includes body dysmorphic disorder (BDD), hoarding disorder, and skin picking (excoriation) disorder (SPD) [2]; a similar grouping will appear in ICD-11 [3]. In determining how to group diagnoses in chapters, DSM-5 authors considered a number of potential criteria, including symptom similarity (phenomenology), comorbidity, familiality, and response to treatment, among others [4].

Classification matters because it can influence how clinicians and researchers think about a condition. For example, it is understandable that the field previously classified BDD as a somatoform disorder, since patients with BDD typically seek general medical and surgical care first, not psychiatric care [5] – perhaps not surprising given the frequent lack of insight in BDD [4]. Nevertheless, BDD appears strongly comorbid with OCD [6], as well as familially and genetically related to OCD [6,7]. In addition, it is helpful to think about BDD as OCD-related since, like OCD [8], BDD appears to respond well to cognitive-behavioral therapy (CBT) with exposure and response prevention (ERP); i.e., the cognitive-behavioral model of OCD seems apt for BDD [9]. Also, like OCD, BDD appears to respond preferentially to potent serotonin reuptake inhibitors compared to placebo and the more noradrenergic agent desipramine [10].

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The change in classification of TTM from an impulse-control disorder to OCD-related has been controversial [9,11]. From a phenomenological perspective, the classification of TTM as OCD-related may be intuitive since both conditions involve a characteristic inability to inhibit or delay behaviors [4]. However, many non-OCD-related conditions include repetitive non-adaptive behaviors, including appetitive conditions like addictions [11]. In addition, while OCD involves compulsive behaviors that reduce distress in the context of obsessions, TTM involves hair pulling in the context of a variety of triggers, including general tension, fatigue, and boredom [11]. Further, though OCD and TTM appear to be strongly comorbid and familially/genetically related to one another [6,7,12–17], their effective treatments differ substantially [11,18]. The form of psychotherapy with the most evidence of efficacy for TTM is habit reversal therapy [11,18], which is quite different from the form of psychotherapy with the most evidence for efficacy in OCD, CBT with ERP [8,11]. Also, unlike in OCD [19], there is little evidence that selective serotonin reuptake inhibitors benefit patients with TTM, though data are limited [18,20].

1.1. Strength of comorbid relationships and classification

The primary objective of the current study was to examine the strength of associations between TTM and other conditions, to inform classification. Though comorbid conditions can relate in a variety of ways, including one condition predisposing to another [11], one potential cause of comorbidity is a common etiology. For example, Krueger examined the strength of associations among common mental conditions in the general population using factor analysis, with the aim of identifying core psychopathological processes underlying these conditions; he noted that anxiety and depressive disorders ("internalizing" conditions) were particularly strongly related to one another [21]. Kendler and colleagues then used multivariate analyses of twin data to determine the potential causes of this comorbidity; the authors concluded that genetic factors in common account for much of the clustering of anxiety and depressive conditions within individuals [22].

Studies of TTM comorbidity to date have been limited by a lack of comparison groups (e.g. [12,13,23–31] with a few exceptions, e.g. [17,32–34]). Similarly, studies of TTM comorbidity to date have been limited by a focus on the prevalence of comorbid conditions [12,13,17,23–33], in contrast to the strength of associations (e.g., odds ratios). Based on prior studies, we can conclude that the most *common* comorbid conditions in TTM are depressive disorders, anxiety disorders, other grooming disorders (e.g., SPD), and substance use disorders [12,13,17,23–34].

In the current study, we examine the *strength* of comorbid associations in persons with TTM in a large, well-phenotyped sample. We had no robust a priori hypotheses regarding which conditions might be most strongly associated with TTM, given limited prior information. However, we considered that TTM might be strongly related to other conditions characterized by impaired impulse control/appetitive behavior, given the differences between OCD and TTM mentioned previously. We emphasize strength of associations over prevalence of comorbid conditions given our sample (enriched for OCD and thus any associated conditions), and because not all psychiatric conditions are equally common in the general population. For example, we would not be surprised if major depressive disorder (MDD) was more common in persons with TTM than anorexia nervosa (AN), even if TTM was more strongly related to AN than to MDD, because MDD is substantially more common than AN in the general population [35,36].

2. Methods

2.1. Sample

We ascertained TTM cases and non-cases for this study through the Johns Hopkins OCD Family Study and the OCD Collaborative Genetics Study (OCGS). TTM cases and non-cases could be probands or controls in the OCD studies. Institutional review boards approved study protocols at each site. All participants provided informed consent after a presentation of study procedures.

2.1.1. The Johns Hopkins OCD Family Study

We recruited adult probands (≥18 years old) from five specialty OCD treatment centers in the Baltimore/Washington area [37]. We rostered all patients with OCD treated in these centers in the three years before the initiation of the study, and we randomly selected 99 patients to participate. We completed interviews for 80 case probands and 343 of their first-degree relatives. We identified control probands using a random-digit dialing procedure, conducted by a survey research contractor (Battelle, Baltimore). We completed Interviews for 73 control probands and 300 of their first-degree relatives.

Probands had to meet DSM-IV criteria for OCD [1] at any time in their lives. Probands could not have schizophrenia, severe mental retardation, Tourette disorder, or OCD occurring exclusively in the context of a major depressive episode (secondary OCD). Participants other than probands had to be at least 7 years old to be in the study.

2.1.2. The OCD Collaborative Genetics Study

The OCGS targeted families with OCD-affected sibling pairs, and extended these when possible through affected first- and second-degree relatives [38]; 487 families participated. We recruited participants from inpatient and outpatient clinics, clinicians in the community, web sites, media advertisements, self-help groups, and Obsessive-Compulsive Foundation annual meetings. We focused recruitment efforts on individuals living in the local area or presenting for treatment at the sites; Johns Hopkins also budgeted resources for ascertainment and evaluation of participants throughout the United States.

2.2. Diagnostic procedures

2.2.1. The Johns Hopkins OCD Family Study

Clinicians (psychiatrists or Ph.D. clinical psychologists) interviewed all participants in person, either in our research offices or in participants' homes. In addition to conducting direct interviews, the clinicians contacted a knowledgeable informant for each participant in order to obtain collateral information for diagnostic clarification. Clinicians with experience evaluating children examined participants between 7 and 15 years old using similar procedures. For participants who had received psychiatric treatment, we sought consent to review relevant medical records and contact treatment providers, if such information was deemed useful for making diagnoses. Examiners completed a narrative formulation for each case.

Diagnostic instruments included the Schedule for Affective Disorders and Schizophrenia-Lifetime Anxiety version (SADS-LA) [39], which we adapted for this study. We adapted the OCD section to include: 1) detailed screening questions; 2) a modified version of the Yale Brown Obsessive Compulsive Scale (YBOCS) symptom checklist [40]; and 3) a modified version of the YBOCS [40]. We developed a similar section for assessing tic disorders. We added sections on BDD; pathological nail biting (PNB), SPD, and TTM (sometimes referred to as pathological grooming conditions or bodily focused repetitive behaviors); and other DSM-IV impulse-control disorders not elsewhere classified: kleptomania, pathological gambling, and pyromania. We operationalized PNB and SPD as impulse-control disorders like TTM in DSM-IV. The probe question for PNB was "Have you ever been unable to stop biting your nails?" That for SPD was "Did you ever pick at your skin, a scab, or scar excessively?" To meet the operational criteria for either condition, there had to be noticeable physical evidence of the behaviors at some point. Additional criteria included 1) an increasing sense of tension immediately before or when attempting to resist the behavior; 2) pleasure, gratification, or relief when performing the behavior; 3) the disturbance was not better accounted for by another mental disorder and not due to a general medical condition; and 4) the disturbance causes clinically significant distress

Table 1
Demographic characteristics of participants with and without lifetime DSM-IV trichotillomania (TTM).

	TTM + ($n = 131$)	TTM − ($n = 2475$)	OR[a] (95% CI)
Age at interview			
5–17 years	23 (18%)	342 (14%)	1.0
18–29 years	38 (29%)	387 (16%)	1.5 (0.8, 2.5)
30–29 years	19 (14%)	412 (17%)	0.7 (0.3, 1.4)
40–49 years	30 (23%)	481 (19%)	0.9 (0.6, 1.6)
50+ years	21 (16%)	852 (34%)	**0.4 (0.2, 0.7)**
Sex			
Male	42 (32%)	1011 (41%)	1.0
Female	89 (68%)	1464 (59%)	**1.5 (1.0, 2.1)**
Ethnicity			
White	123 (95%)	2381 (97%)	1.0
Other	6 (5%)	82 (3%)	1.4 (0.7, 3.0)
Education			
Less than high school	29 (22%)	562 (23%)	1.0 (0.5, 1.7)
High school graduate	12 (9%)	256 (10%)	0.9 (0.4, 1.8)
Some College	29 (22%)	571 (23%)	0.9 (0.5, 1.7)
College graduate	38 (29%)	646 (26%)	1.1 (0.6, 2.0)
Advanced degree	23 (18%)	425 (17%)	1.0
Yearly household income			
$0–19,999	16 (14%)	225 (11%)	1.0
$20,000–39,999	25 (22%)	356 (17%)	1.0 (0.5, 1.8)
$40,000–59,999	15 (13%)	410 (20%)	0.5 (0.3, 1.0)
$60,000–79,999	17 (15%)	335 (16%)	0.7 (0.4, 1.4)
$80,000–99,999	13 (12%)	258 (12%)	0.7 (0.3, 1.5)
$100,000+	26 (23%)	514 (24%)	0.7 (0.4, 1.3)
Highest occupational status			
Unskilled or unemployed	35 (27%)	482 (20%)	1.4 (0.8, 2.3)
Skilled manual employee	6 (5%)	97 (4%)	1.2 (0.5, 2.7)
Clerical/sales/technical employee	32 (25%)	673 (28%)	0.9 (0.5, 1.5)
Administrator	23 (18%)	554 (23%)	0.8 (0.4, 1.4)
Executive/professional	33 (26%)	615 (25%)	1.0

[a] Odds ratio (OR) and 95% confidence interval (CI) calculated using generalized estimating equations logistic regression; **bolded** if statistically significantly different than 1.0, $p < 0.05$.

or impairment in social, occupational, or other important areas of functioning [41,42]. We adapted the Family Informant Schedule and Criteria [43] to interview collateral informants. We evaluated children using comparable age-appropriate instruments (i.e., the Kiddie-Schedule for Affective Disorders and Schizophrenia [44] and Child Y-BOCS [45]). We completed a Diagnostic Assignment Checklist form for every participant.

Two expert psychiatrists reviewed all available diagnostic materials (clinical case summary, evaluation by the clinical examiner, informant interview, medical records, and audiotapes) to make DSM-IV diagnoses by consensus.

2.2.2. The OCD Collaborative Genetics Study

Clinicians (psychiatrists or Ph.D. clinical psychologists) who had experience with clinical evaluations conducted diagnostic assessments. To evaluate OCD, tic disorders, and the previously mentioned DSM-IV impulse-control disorders, clinicians used the same instrument as in the OCD Family Study. Clinicians used the Structured Clinical Interview for DSM-IV [46] to assess other Axis I diagnoses.

At each site, two expert diagnosticians independently reviewed materials for each case and completed a Diagnostic Assignment Checklist form using DSM-IV criteria. The two diagnosticians resolved any disagreements between themselves. One of the five consensus psychiatrists at JHU then reviewed the materials. We resolved any disagreements between other sites and JHU before we edited the case materials and sent them for data entry.

2.3. Statistical analysis

We conducted all statistical analyses using SPSS v 25. We performed logistic regressions using generalized estimating equations (to account for within-family associations) to measure associations between TTM and demographic factors, and between TTM and other lifetime DSM-IV disorders [47]. We adjusted for potential demographic confounders, then OCD, when computing adjusted odds ratios (ORs) relating TTM to other disorders. Our primary interest was in the strength of associations (i.e., the magnitude of ORs) between TTM and other disorders. For the purposes of the current study, we considered ORs statistically significantly different from unity if $p < 0.05$, recognizing that the prior probabilities that some of these ORs would be >1 were relatively high (e.g., that relating TTM to MDD [12,18,48]), but also recognizing the potential of false positive results given multiple tests (21 potential comorbid conditions of interest). Thus, we also indicate whether relationships between TTM and other DSM-IV disorders are statistically significant after correction for multiple testing using the very conservative Bonferroni method ($\alpha = 0.05/21 = 0.0024$).

Table 2
Lifetime prevalence of other DSM-IV disorders in participants with and without lifetime trichotillomania (TTM).

Disorder	TTM+ ($n = 131$)	TTM- ($n = 2475$)	OR[a] (95% CI)	OR[b] (95% CI)	OR[c] (95% CI)
Any tic disorder	29 (23%)	303 (13%)	**2.0 (1.4, 3.1)***	**1.9 (1.2, 2.9)**	1.4 (0.9, 2.2)
Alcohol dependence	26 (20%)	307 (13%)	**1.8 (1.1, 2.8)**	**1.9 (1.2, 3.2)**	**1.7 (1.0, 2.9)**
Illicit drug dependence	16 (12%)	184 (8%)	1.7 (0.9, 3.2)	1.7 (0.9, 3.1)	1.6 (0.8, 3.0)
Major depressive disorder	81 (64%)	1111 (46%)	**2.1 (1.4, 3.0)***	**1.9 (1.3, 2.8)***	1.3 (0.9, 2.0)
Dysthymic disorder	24 (20%)	279 (12%)	**1.8 (1.2, 2.9)**	**1.8 (1.2, 3.0)**	1.4 (0.9, 2.3)
Bipolar disorder (I or II)	12 (9%)	115 (5%)	**2.1 (1.1, 4.1)**	1.9 (1.0, 3.8)	1.4 (0.8, 2.9)
Separation anxiety disorder	25 (21%)	392 (17%)	1.3 (0.9, 2.1)	1.0 (0.6, 1.6)	0.8 (0.5, 1.2)
Panic disorder	20 (16%)	307 (13%)	1.3 (0.8, 2.0)	1.2 (0.7, 1.9)	0.8 (0.5, 1.4)
Agoraphobia	18 (14%)	233 (10%)	1.5 (0.9, 2.6)	1.4 (0.9, 2.4)	1.0 (0.6, 1.8)
Specific phobia	59 (46%)	795 (33%)	**1.7 (1.2, 2.5)**	**1.6 (1.1, 2.4)**	1.4 (0.9, 2.1)
Social phobia	63 (51%)	795 (33%)	**2.1 (1.4, 3.1)***	**2.0 (1.4, 2.9)***	**1.6 (1.1, 2.4)**
Obsessive-compulsive disorder	110 (87%)	1297 (53%)	**5.6 (3.2, 9.8)***	**4.7 (2.7, 8.4)***	–
Generalized anxiety disorder	64 (52%)	694 (29%)	**2.7 (1.8, 3.8)***	**2.5 (1.7, 3.6)***	**1.8 (1.2, 2.7)***
Body dysmorphic disorder	12 (10%)	170 (7%)	1.4 (0.8, 2.6)	1.2 (0.6, 2.2)	0.8 (0.4, 1.5)
Anorexia nervosa	6 (5%)	75 (3%)	1.5 (0.7, 3.5)	1.1 (0.5, 2.6)	0.9 (0.4, 2.2)
Bulimia nervosa	10 (8%)	57 (2%)	**3.5 (1.7, 7.4)***	**2.7 (1.2, 5.8)**	**2.2 (1.0, 4.6)**
Pathological nail biting	46 (36%)	345 (14%)	**3.4 (2.4, 4.9)***	**3.1 (2.2, 4.5)***	**2.8 (2.0, 4.1)***
Skin picking disorder	55 (44%)	369 (15%)	**4.4 (3.0, 6.5)***	**3.9 (2.6, 5.7)***	**3.1 (2.0, 4.7)***
Kleptomania	12 (9%)	38 (2%)	**6.6 (3.4, 13)***	**6.0 (3.2, 11)***	**4.9 (2.6, 9.2)***
Pathological gambling	3 (2%)	21 (1%)	2.8 (0.8, 9.2)	**3.8 (1.1, 13)**	3.2 (1.0, 11)
Pyromania	5 (4%)	17 (1%)	**5.8 (2.2, 15)***	**4.6 (1.7, 12)**	**3.9 (1.4, 11)**

[a] Odds ratio (OR) and 95% confidence interval (CI) calculated using generalized estimating equations logistic regression; **bolded** if statistically significantly >1.0, $p < 0.05$; *$p < 0.0024$.
[b] OR and 95% CI calculated using generalized estimating equations logistic regression, adjusted for age group and sex; **bolded** if statistically significantly >1.0, $p < 0.05$; *$p < 0.0024$.
[c] OR and 95% CI calculated using generalized adjusted for age group, sex, and obsessive-compulsive disorder; **bolded** if statistically significantly >1.0, $p < 0.05$; *$p < 0.0024$.

3. Results

3.1. TTM demographic correlates

We identified 131 participants with lifetime TTM, 5% of the sample (total $n = 2606$). The median age at onset of TTM was 13 years. Younger age at interview and female sex were associated with TTM (Table 1).

3.2. TTM comorbidity

Table 2 shows the lifetime prevalence of other DSM-IV disorders in participants with and without TTM. In unadjusted analyses, TTM had excess comorbidity with a number of conditions from different DSM-IV chapters, including tic disorders, alcohol dependence, mood disorders (MDD, dysthymia, and bipolar disorder), anxiety disorders (specific phobia, social phobia, OCD, and generalized anxiety disorder [GAD]), impulse-control disorders not elsewhere classified (PNB and SPD; kleptomania, pathological gambling, and pyromania), and bulimia nervosa. Of these, the conditions with the highest prevalences in participants with TTM were OCD (87%), MDD (64%), GAD (52%), social phobia (51%), specific phobia (46%), SPD (44%), PNB (36%), tic disorders (23%), alcohol dependence (20%), and dysthymic disorder (20%). However, the prevalences of many of these conditions were also high in participants without TTM in this OCD-enriched sample – especially OCD itself (53%), MDD (46%), social phobia (33%), specific phobia (33%), and GAD (29%).

Fig. 1 illustrates the strength of associations between TTM and other DSM-IV disorders. Unadjusted ORs were highest for kleptomania (6.6), pyromania (5.8), OCD (5.6), SPD (4.4), bulimia nervosa (3.5), and PNB (3.4).

Adjusting for age group and sex tended to weaken relationships between TTM and other DSM-IV disorders, though the relationship between TTM and pathological gambling became stronger (Table 2). Additionally adjusting for OCD weakened the relationships between TTM and most disorders further; however, the relationships between TTM and most DSM-IV impulse-control disorders remained strong (Table 2). Notably, with adjustment the *relative* strength of associations between TTM and other disorders did not change appreciably (e.g., the OR relating TTM and SPD remained larger than the OR relating TTM and GAD).

4. Discussion

In this study of >2600 well-phenotyped participants from OCD family and genetic studies, we found that TTM was most strongly associated with OCD and other conditions previously conceptualized as impulse-control, appetitive disorders. Adjusting for demographic correlates of TTM and OCD did not substantially alter these results. Though DSM-5 includes TTM as an OCD-related disorder, its comorbidity pattern also emphasizes the impulsive, appetitive aspects of this condition that may be relevant to classification.

As expected in a sample enriched for OCD and thus related conditions, TTM was relatively common, affecting 5% of participants (i.e., relatively common compared to prior estimates of 0.6–1% in samples less selected for psychiatric morbidity [49,50]). Consistent with prior literature [48], we found that the median age of onset for TTM was 13 years, and TTM was more common in females.

4.1. Comorbidity, familiality, and the genetic basis of DSM-5 OCD-related disorders

In a prior study, our group employed the current sample but analyzed OCD comorbidity and familiality using a family study design – i.e., examining comorbidity and familiality in case versus control probands and first-degree relatives, respectively [6]. The other conditions most strongly *comorbid* with OCD, in order, were GAD, panic disorder, tic disorders, agoraphobia, TTM, SPD, BDD, bipolar disorders, MDD, dysthymic disorder, and separation anxiety disorder (all ORs >3). The other conditions most *familially* related to OCD, in order, were agoraphobia, GAD, TTM, BDD, tic disorders, SPD, dysthymic disorder, panic disorder,

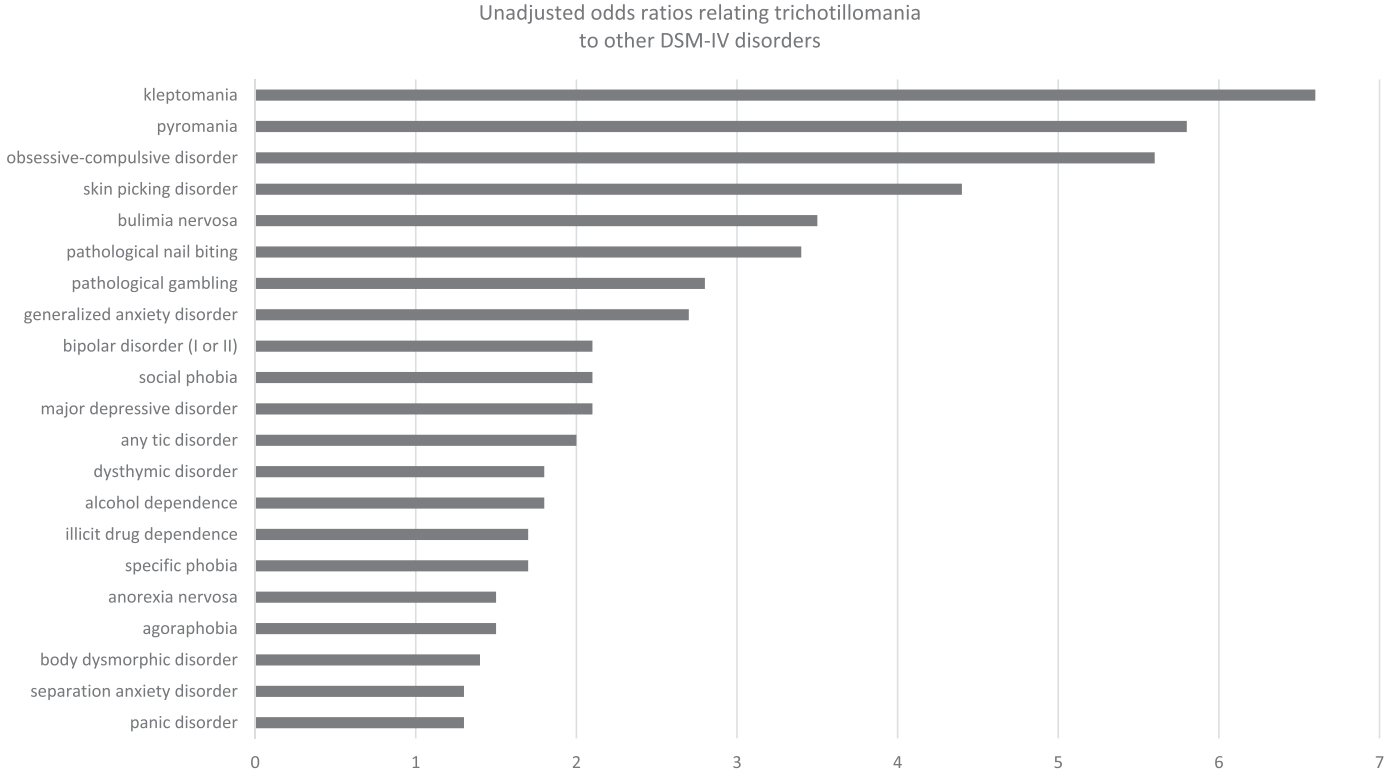

Fig. 1. Strength of associations between trichotillomania and other DSM-IV disorders.

and separation anxiety disorder (all ORs ≥3). Thus, based on strength of comorbid associations and familiality, OCD could be classified with other DSM-IV anxiety disorders, TTM, BDD, tic disorders, SPD, and mood disorders [6].

In contrast, in the current study, the other conditions most strongly associated with TTM were, in order, kleptomania, pyromania, OCD, SPD, bulimia nervosa, and PNB (all ORs >3). Thus, based on strength of comorbid associations, TTM could be classified as a condition involving impaired impulse control/appetitive behavior, an OCD-related disorder, or a grooming disorder. Since we know relatively little about the strength of associations between the DSM-IV conditions referred to as impulse control disorders not elsewhere classified – with each other and with other conditions – this area is ripe for future studies.

Notably, TTM was not statistically significantly associated with the other DSM-5 OCD-related condition we assessed in the current study, BDD. The lifetime prevalence of BDD was high (10%) in those with TTM, but it was also high (7%) in those without TTM in this OCD-enriched sample.

Interestingly, in a large multivariate female twin study of DSM-5 obsessive-compulsive and related disorder dimensions, Monzani and colleagues reported that the best-fitting model included *two* latent factors [7]. The first factor included OCD, BDD, hoarding disorder, TTM and SPD, and the second factor only included TTM and SPD. Though all of the conditions were genetically related to OCD, TTM and SPD appeared less so. In addition, TTM and SPD shared genetic influences that were not shared with OCD, hoarding disorder, and BDD [7]. Thus, based on comorbidity, familiality, and twin research, TTM appears both similar to and different from OCD.

4.2. Strengths and limitations

Strengths of the current study include the large sample size and rigorous diagnostic methods. Though having an OCD-enriched sample was a strength in that a relatively large proportion (5%, 131 participants) had TTM, the prevalence of OCD in those with TTM was unusually high. Nevertheless, controlling for OCD had little effect on the relative strength of associations between TTM and other disorders. Another limitation was that we used overly restrictive DSM-IV criteria to evaluate and diagnose TTM, and it is unclear how our results might differ had we measured the more inclusive DSM-5 conception of TTM. We also adapted DSM-IV TTM criteria to evaluate and diagnose SPD and PNB, though SPD in DSM-5 is similarly a more inclusive diagnosis. Finally, the DSM-IV criteria for pathological gambling were a bit less inclusive than the DSM-5 criteria for gambling disorder, limiting statistical power and our confidence in our pathological gambling results.

4.3. Conclusions

TTM is comorbid with a number of psychiatric conditions besides OCD, and it is strongly associated with other conditions involving impaired impulse control. Though DSM-5 includes TTM as an OCD-related disorder, its comorbidity pattern also emphasizes the impulsive, appetitive aspects of this condition that may be relevant for classification.

Declaration of Competing Interest

None.

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