Title

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Journal

European Child & Adolescent Psychiatry, 27(5)

ISSN

1018-8827

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Publication Date

2018-05-01

DOI

10.1007/s00787-017-1074-z

Peer reviewed

HHS Public Access

Author manuscript

Eur Child Adolesc Psychiatry. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

Eur Child Adolesc Psychiatry. 2018 May ; 27(5): 569–579. doi:10.1007/s00787-017-1074-z.

Prevalence and Predictors of Hair Pulling Disorder and Excoriation Disorder in Tourette Syndrome

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ETHICAL STANDARDS

All research subjects provided written informed consent (written assent was obtained for individuals <18 along with written parental consent). The study was approved by the relevant IRBs/ethics committees at all sites, and therefore have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

CONFLICT OF INTERESTS

Drs. Sandor, Dion, Lyon, King, Budman, Grados, Pauls, Mathews and Scharf have received research support from the Tourette Association of America (TAA). Dr. Budman reports funding for clinical research studies from Neurocrine Pharmaceuticals, Psyadon Pharmaceuticals, Otsuka Pharmaceuticals, Synchroneuron Pharmaceuticals, Teva Pharmaceuticals, and Auspex Pharmaceuticals. She has also been a speaker for the TAA and the Center for Disease Control Partnership and a consultant to Bracket. Dr. Sandor reports unrestricted educational grants from Purdue and Shire, a speaker fee from Purdue, and support for clinical research from Otsuka Pharmaceuticals. Dr. Sandor was also a member of the data safety monitoring committee for Psyadon Pharmaceuticals. Drs. Pauls, Keuthen and Scharf have received grant support from the TLC Foundation for Body-Focused Repetitive Behaviors (BFRBs). Drs. Keuthen and Scharf are members of the Scientific Advisory Board of the TLC Foundation for BFRBs. Dr. Scharf has also received consulting fees from Nuvelation Pharma, travel and grant support from the TAA, and is a member of the Scientific Advisory Board for the TAA. Dr. Mathews has received research support, honoraria, and travel support from the TAA and is the co-chair of the TAA Scientific Advisory Board. Drs. Greenberg, Illmann, Darrow, Hirschtritt, and Ms. Tung, Gauvin, Osiecki, Yang, Curley and Essa report no biomedical financial interests or potential conflicts of interest.

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Abstract

Objective—Trichotillomania/hair pulling disorder (HPD) and excoriation/skin picking disorder (SPD) are childhood-onset, body-focused repetitive behaviors that are thought to share genetic susceptibility and underlying pathophysiology with obsessive-compulsive disorder (OCD) and Tourette syndrome (TS). We sought to determine the prevalence of *DSM-5* HPD and SPD in TS patients, and to identify clinical factors most associated with their co-morbidity with TS.

Method—Participants included 811 TS patients recruited from TS specialty clinics for a multi-center genetic study. Patients were assessed using standardized, validated semi-structured interviews. HPD and SPD diagnoses were determined using a validated self-report questionnaire. HPD/SPD prevalence rates were calculated, and clinical predictors were evaluated using regression modeling.

Results—3.8% and 13.0% of TS patients met *DSM-5* criteria for HPD and SPD, respectively. In univariable analyses, female sex, OCD, and both tic and obsessive-compulsive severity were among those associated with HPD and/or SPD. In multivariable analyses, only lifetime worst-ever motor tic severity remained significantly associated with HPD. Female sex, co-occurring OCD, ADHD and motor tic severity remained independently associated with SPD.

Conclusion—This is the first study to examine HPD and SPD prevalence in a TS sample using semi-structured diagnostic instruments. The prevalence of HPD and SPD in TS patients, and their association with increased tic severity and co-occurring OCD, suggests that clinicians should screen children with TS and related disorders for HPD/SPD, particularly in females and in those with co-occurring OCD. This study also helps set a foundation for subsequent research regarding HPD/SPD risk factors, pathophysiology, and treatment models.

Keywords

Trichotillomania/Hair Pulling Disorder; Excoriation Disorder/Skin Picking Disorder; Tourette syndrome; Obsessive-Compulsive Disorder; Body-Focused Repetitive Behaviors; tics

INTRODUCTION

Body-focused repetitive behaviors (BFRBs) are potentially debilitating, pathological repetitive behaviors that target one or more body regions, and include problematic hair pulling, skin picking, and nail biting [1–3]. Here, we focus on two BFRBs, trichotillomania/hair pulling disorder (HPD) and excoriation/skin picking disorder (SPD), which are included

in the *DSM-5* within the obsessive-compulsive related disorders (OCRD) chapter [4]. HPD and SPD are characterized by recurrent hair pulling (or skin picking) resulting in hair loss (or skin lesions), the inability to stop pulling/picking, and associated significant distress or functional impairment.

DSM-5 HPD is hypothesized to affect 1–2% of the population [4]; however, HPD prevalence has been difficult to characterize given the lack of large-scale epidemiological studies and the use of inconsistent diagnostic criteria across existing reports [5]. As such, HPD prevalence estimates have ranged from 0.6% for both sexes combined using strict *DSM-III-R* criteria to 1.5% of males and 3.4% of females using less stringent criteria [6]. *DSM-IV* HPD prevalence is thought to be about 1% [5]. While the gender distribution of HPD in the community varies across studies, the clinical HPD population tends to be primarily female [5, 7].

SPD prevalence has been similarly challenging to estimate, given its changing definition over time and its absence in the *DSM* until the most recent version, *DSM-5*, published in 2013 [4]. Prior to 2013, studies of non-clinical samples have reported prevalence rates ranging from 1.4–5.4% [8–10]; current *DSM-5* estimates range as high as 7.7% [11]. As in HPD, SPD is also believed to affect more women than men [12].

Both HPD and SPD are typically early adolescent-onset conditions. While HPD age of onset is fairly uniform, usually occurring between ages 11–14 [7], SPD onset varies more substantially, with three reported peaks of onset: age<10, 13–15, and 30–45 [8]. HPD and SPD show increased co-morbidity with one another [7, 13, 14], and a large population-based twin study demonstrated that HPD and SPD have a significant proportion of shared heritability as well [14]. Both disorders also have shared heritability and presumably overlapping pathophysiology with OCD, and thus have been included as obsessive-compulsive related disorders (OCRDs) in *DSM-5* [14]. Like OCD, patients with HPD and/or SPD find it difficult to resist behaviors/rituals despite aversive consequences [5, 8]. OCD patients also tend to have elevated rates of HPD and SPD compared to controls, and these BFRBs occur more frequently in relatives of OCD probands than in relatives of controls [14–21].

However, the relationship between BFRBs and Tourette syndrome (TS) is less well understood. TS is a childhood-onset neuropsychiatric disorder characterized by multiple motor tics and at least one vocal tic present for at least one year in duration [4]. TS, BFRBs and OCD share multiple characteristics and etiological features, including repetitive, impulsive and compulsive behaviors, dysregulated habit formation, proposed overlapping pathophysiology attributed to frontostriatal dysfunction, and impaired inhibition of motor responses [2, 22, 23]. In fact, many researchers categorize TS as an OCRD for both research and clinical purposes, based on shared characteristics, genetic relationships, and psychobiological overlap [2, 15, 17, 23].

The few existing studies of TS and HPD have generally found increased HPD rates in TS patients, including one that examined *DSM-IV*-based HPD diagnoses and reported a rate of 2.6% [3, 24, 25]. However, prior studies have been limited by the absence of formal

diagnostic instruments, and/or did not examine whether the higher rates of HPD in TS patients are seen only when OCD is also present, or whether there might be a more direct relationship between TS and HPD independent of OCD [2, 22, 26–28]. Even less is known about SPD in TS. Outside of increased rates of skin picking reported in a sample of OCD patients with tic disorders compared to OCD patients without tics, the prevalence of SPD in TS patients has not, to our knowledge, been examined [29].

Developing a better understanding of the relationship between BFRBs and TS has both potential diagnostic and treatment implications. If studies were to suggest a stronger association between TS and BFRBs compared to OCD and BFRBs, they might change how these repetitive disorders are taught, organized and conceptualized, especially given that BFRBs are currently characterized as OCRDs, separate from TS. An improved understanding of the clinical phenomenology of HPD and SPD may also help to generate hypotheses about the underlying pathophysiologic mechanisms of BFRBs and to guide future genetic, imaging and other etiological studies [30]. Clarifying these relationships could also impact treatment approaches, as OCD and TS respond to different pharmacological interventions (i.e. selective serotonin reuptake inhibitors in OCD, neuroleptics in TS).

Therefore, the goals of this study were to (1) characterize HPD and SPD in a TS sample, and (2) to determine which factors, if any, are associated with the presence of HPD or SPD in TS-affected patients. In particular, we were interested in whether BFRBs in TS could be attributed to co-occurring OCD, other co-morbidities or clinical factors; or conversely, whether the relationship might be more directly associated with TS. We hypothesized that (1) both HPD and SPD rates would be increased in TS patients compared to that in the general population and (2) that elevated HPD/SPD rates would be only partially explained by the presence of co-occurring OCD.

METHODS

Patients

Patients with *DSM-IV-TR*-defined TS (N=811) and data on hair pulling and skin picking behaviors were included in this study. Patients were recruited from TS specialty clinics in the US and Canada as part of a larger multi-site genetic study [31, 32]. All patients provided written informed consent (written assent was obtained for individuals <18 along with written parental consent). Patients <18 who completed the questionnaires typically did so with the assistance of their parents. Patients with existing diagnoses of developmental delay or intellectual disability were excluded. The study was approved by the relevant IRBs at all sites.

Diagnoses

Patients were assessed using a standardized, semi-structured instrument developed by the Tourette Association of America International Consortium for Genetics (TAAICG) (formerly known as the TSAICG), the Tic and Co-morbid Symptom (TICS) Inventory, which has previously been demonstrated to be valid and reliable for diagnoses of TS, OCD,

and attention deficit hyperactivity disorder (ADHD) [32, 33]. Interview questions included demographic information, tic and obsessive-compulsive severity scales and symptom checklists modified from the Yale Global Tic Severity Scale (YGTSS), the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), and the Swanson Nolan and Pelham Parent and Teacher Rating Scale for ADHD, version 4 (SNAP-IV) [34–36]. Clinical lifetime diagnoses of TS, OCD, and ADHD were determined by TS clinical research experts using a best-estimate consensus approach [33]. Only patients who met *DSM-IV*-TR TS criteria, and had available HPD, SPD, OCD, and ADHD data were included in the analyses. Reliable information about medication status was not available.

Patients were assessed for lifetime HPD and SPD using a self-report screening questionnaire on Body-Focused Repetitive Behaviors (BFRBs) contained within the TICS Inventory (BFRB questionnaire; see Online Resource 1, Figure S1). This questionnaire was initially designed for genetic and family studies of childhood-onset OCD [18], and includes separate questions on a) lifetime presence of hair pulling and/or skin picking, b) the ability (or inability) to stop pulling hair/picking skin, c) whether these behaviors ever resulted in bald spots, noticeable hair loss, scabbing, or infections, d) the presence of tension and/or relief associated with completion of the behavior, and e) questions assessing age of onset, impairment, distress, and effects on important relationships. Though the questionnaire was developed prior to the advent of the *DSM-5*, it includes all criteria needed to establish both *DSM-IV* and *DSM-5* diagnoses (Online Resource 1, Figure S1). We established the validity of the BFRB self-report questionnaire for determining *DSM-5* HPD and SPD diagnoses using an independent sample of 78 HPD patients and 183 first-degree relatives of HPD patients recruited for HPD genetic and family studies [13]. For validating *DSM-IV* diagnoses, 97 HPD cases and 47 unaffected controls from the HPD family study were used (Online Resource 1). *DSM-IV* and *DSM-5* HPD diagnoses were determined using a best-estimate consensus approach by two independent raters using only the BFRB questionnaire (Online Resource 1). *DSM-5* SPD diagnoses were assigned, as were "*DSM-IV* equivalent" SPD diagnoses based on previously published criteria to facilitate comparisons (Online Resource 1, Figure S2) [37]. Kappa coefficients comparing diagnoses derived from the BFRB questionnaire versus gold-standard diagnostic interviews were 0.93 and 0.77 for *DSM-5* HPD and SPD, respectively; kappa coefficients for *DSM-IV* HPD and *DSM-IV*-equivalent SPD were 0.85 and 0.91, respectively (Online Resource 1, Table S1).

Analyses

All statistical analyses were performed in Stata v12 (StataCorp, College Station, TX). Candidate HPD/SPD clinical predictors, selected based on the literature, included: age, sex, co-occurring OCD or ADHD, TS and OCD age of onset, family history of TS and/or OCD and worst-ever YGTSS and Y-BOCS scores. Univariable logistic regression was used to determine odds ratios and 95% confidence intervals (CI) for categorical and continuous predictor variables. Wilcoxon rank-sum tests were used to compare differences for non-normally distributed continuous variables, including age at interview and ages of onset. Fisher's exact test was used to examine differences in HPD/SPD prevalence rates among children (≤12), adolescents (13–17) and adults (≥18). Candidate predictors with $p<0.10$ in univariable analyses were considered for inclusion in the final multivariable regression

model. Age at time of interview was included in the final models to control for younger patients who had not yet passed through the BFRB developmental period of risk. For the final models, variables were considered to be independently associated with HPD and/or SPD at a threshold of $p<0.05$. All statistical tests were two-tailed. If more than one tic-related severity score was associated with the outcome of interest, only the most highly associated score was included in the multivariable analyses to limit confounding. Similarly, to increase power, family history of TS and OCD was examined as a joint variable, since the number of subjects with a positive family history of each disorder separately was small, particularly in the HPD+ sample, and because prior data suggests that OCD in relatives of TS probands may arise from a genetic susceptibility for TS [38]. Co-linearity between all predictor variables was assessed in post-hoc analyses by calculating their variance inflation factors (VIFs). Variables with a VIF>10 were considered to be co-linear. When variables were found to be co-linear, the variable with the strongest univariate relationship with the outcome variable was used in multivariable calculations; all others were removed from the model.

RESULTS

Sample Characteristics

77% (n=628) of TS patients were male; the average age of TS onset was 6.1 years (SD 2.7) (Table 1). 53% (n=422) and 48% (n=372) met *DSM-IV* criteria for OCD and ADHD, respectively. 54% (n=425) of TS patients had a family history of OCD and/or TS. The average YGTSS total tic score was 31.4/50 (SD 8.3), consistent with moderately severe TS. Of those with OCD, the average Y-BOCS score was 23.9/40 (SD 7.2), consistent with moderately severe OCD.

2.6% (n=20) and 3.8% (n=29) of TS patients met *DSM-IV* and *DSM-5* diagnostic criteria for HPD, respectively. Females had approximately twice the rate of HPD as males using either diagnostic criteria (6.4% vs. 3.0%, respectively, for *DSM-5* HPD, ($\chi^2(1)=4.3$, $p=0.04$); 4.7% vs. 2.0% for *DSM-IV*-TR HPD ($\chi^2(1)=3.7$, $p=0.05$). The median age of HPD onset was 12.8 years (IQR, 7–16; Online Resource 1, Figure S3). When stratified by age of interview, 1.6% of children met *DSM-5* criteria for HPD, compared to 3.5% of adolescents, and 6.4% of adults ($p=0.01$; Online Resource 1, Table S2). Similarly, comparing all children <18 to adults, 2% met DSM-5 criteria for HPD compared to 6.4% of adults ($p=0.005$) (Online Resource 1, Table S3).

13.0% (n=101) met *DSM-5* criteria for SPD. As with HPD, females had approximately a 2-fold increase in rates of *DSM-5* SPD compared to males (19.7% vs. 11.1%, ($\chi^2(1)=8.7$, $p=0.003$). The mean age of SPD onset was 8.3 years (SD 3.7) (Online Resource 1, Figure S3). Age of onset between males and females did not differ for either HPD or SPD (Mann-Whitney U $Z=1.2$, $p=0.24$ and $t=0.02$, $p=0.98$, respectively). Unlike HPD, there were no significant differences in SPD rates between children (10%), adolescents (15.8%) and adults (14.2%) ($p=0.12$) (Online Resource 1, Table S2), or between those ages <18 (12%) compared to those ≥18 (14%) ($p=0.47$) (Online Resource 1, Table S3). Of those with HPD, 35% (n=9) of patients had SPD; of those with SPD, 9.4% (n=9) had HPD.

HPD Univariable Analyses

In TS patients meeting *DSM-5* HPD criteria, female sex, co-occurring SPD, higher YGTSS total tic score, higher YGTSS motor tic score, higher Y-BOCS total score, co-occurring OCD, and a family history of TS and/or OCD were associated with HPD at p≤0.10 (Table 2). Given its stronger association with HPD in the univariable analyses, YGTSS motor tic score rather than YGTSS total tic score was included in the multivariable analysis.

HPD Multivariable Analysis

In the final multivariable model, only YGTSS motor score remained significantly associated with increased risk of HPD (14% increased risk for every 1 point increase in YGTSS motor tic severity; p=0.04) (Table 3). Females with TS had nearly twice the odds of co-occurring HPD compared to males, though this association did not surpass nominal significance (OR=1.97, 95%CI: 0.81–4.80, p=0.14) (Table 3). To examine whether these results might have been driven primarily by either the child or adult TS subgroups alone, we conducted a sensitivity analysis by stratifying the sample into children and adults and repeating the multivariable regression analyses in each age group separately. The results of these stratified analyses were generally consistent across both pediatric and adult subgroups (Online Resource 1, Table S4).

SPD Univariable Analyses

In the univariable analyses, female sex, increased YGTSS scores, co-occurring OCD, OCD age of onset, increased Y-BOCS score, co-occurring HPD, co-occurring ADHD, a positive family history of HPD, and a positive family history of either TS or OCD met pre-specified criteria (p<0.10) for inclusion in the multivariable model (Table 4).

SPD Multivariable Analysis

In the SPD multivariable analysis, female sex, co-occurring OCD, ADHD, YGTSS motor score, and a positive family history of either TS or OCD all remained significantly associated with increased SPD risk in TS patients (Table 5). To examine whether these results might have been driven primarily by either the child or adult TS subgroups alone, we conducted a sensitivity analysis by stratifying the sample into children and adults and repeating the multivariable regression analyses in each age group separately. The results of these stratified analyses were generally consistent across both pediatric and adult subgroups (Online Resource 1, Table S4).

Because OCD age of onset and Y-BOCS score are dependent on positive OCD diagnoses, and would thus be collinear with OCD in a multivariable regression, they were not included in the final SPD multivariable regression model. However, a secondary analysis restricted to TS patients with co-occurring OCD demonstrated that OCD age of onset was also an independent predictor of SPD, with younger age of onset associated with higher risk (OR=0.86, 95% CI: 0.78–0.95, p=0.004), while Y-BOCS score was not (OR=1.02, 95% CI: 0.98–1.07, p=0.25) (Online Resource 1, Table S6).

DISCUSSION

The primary aims of this study were to determine prevalence rates and clinical predictors of HPD and SPD in patients with Tourette syndrome (TS). We sought to clarify whether the occurrence of these BFRBs in TS might be mediated by a shared co-morbidity with OCD or whether BFRBs may be associated with TS independent of co-occurring OCD. This study expands on the current literature in two ways: 1) the use of a structured, systematic assessment of BFRBs in a large sample of well-characterized TS patients using a validated, brief self-report questionnaire; 2) the examination of SPD, which to date has not been studied in TS.

In this TS sample, 3.8% of patients met *DSM-5* HPD criteria. While the population prevalence of *DSM-5* HPD has not yet been established, preliminary estimates range from 1–2%, suggesting that our sample had twice the presumed population prevalence of HPD [4]. The *DSM-IV* HPD rate of 2.6% observed here in TS patients is also more than twice the reported *DSM-IV* HPD population prevalence of 1% [5], and comparable to the estimate of 2.6% from an international TS clinical registry [3]. Although previously reported rates are more variable for SPD, the 13% SPD prevalence rate found in this study represents a nearly two-fold increase over the highest reported estimates in non-clinical samples based on *DSM-5* criteria (7.7%) [11], and a two-to-nine-fold increase over the more commonly accepted population rates of 1.4–5.4%. Given that HPD/SPD rates were higher in adolescent and adult TS patients than in children (Online Resource 1, Table S2; Figure S3), consistent with prior reports of an HPD and SPD peak onset in early adolescence [7, 8], these estimates may be conservative. Of note, prior studies systematically assessing OCD patients and controls for *DSM-IV* HPD and *DSM-IV*-equivalent SPD [37] using the same BFRB questionnaire found similar, though notably higher, rates of HPD and SPD in OCD patients (HPD: 11% of OCD patients vs. 1% controls; SPD: 31% OCD patients vs. 6% controls) [18, 19, 39]. Both HPD and TS are also found more frequently in early-onset than in later-onset OCD [40, 41]. These data suggest that TS may have a similar biological (possibly genetic) relationship with HPD and SPD as previously demonstrated for HPD/SPD and OCD [14]. In this context, it is also worth noting that both tics and BFRBs can be influenced by internal (e.g. anxiety, excitement) and external (e.g. homework, classroom) environmental states [7].

Prior studies have repeatedly demonstrated that HPD and SPD co-occur more frequently than expected by chance [7]. Heritability analyses in a large UK twin sample found that, in addition to a genetic liability factor that was shared across all studied OCRDs (HPD, SPD, OCD, hoarding disorder and body dysmorphic disorder), a second genetic liability factor loaded exclusively on HPD and SPD [14]. Findings in our sample, where 35% of patients with HPD had SPD, and 9.4% with SPD had HPD, are consistent with these findings, and provide further support for grouping HPD and SPD together as related disorders in *DSM-5*. The significant association between SPD and family history of OCD or TS also supports the notion of shared heritability across these BFRBs, OCD, and TS [14, 18, 42].

As seen in previous clinical samples, females in the current study were twice as likely as males to have HPD and/or SPD, though the relationship between female sex and HPD was not significant in the multivariable analysis. Given the small number of patients that met

DSM-5 HPD criteria, and the 3:1 ratio of males to females (as would be expected in a clinical TS population) [3], our sample is likely underpowered to detect significant differences by sex in multivariable models. Recent studies have also proposed that the previously observed female predominance in HPD patients might be a function of treatment-seeking bias, rather than an actual increased female-to-male prevalence in the general population [7]. Other studies have reported that childhood-onset HPD may be more sex equal, and that male hair-pullers tend to have more tics than females [17, 43]. However, as the patients in our study were not ascertained based on seeking treatment for HPD, female sex appears to represent a major risk factor for HPD and SPD in TS patients.

While female sex had a consistent relationship with both HPD and SPD, patterns of association with other clinical variables differed between the two disorders in our sample. In the multivariable analyses, YGTSS motor tic score was the only predictor significantly associated with both higher HPD and SPD rates. In contrast, co-occurring OCD, younger age of OCD onset, and ADHD were all significantly associated with SPD, but not HPD. The strongest SPD predictor was OCD: TS patients with co-occurring OCD had four times the odds of meeting *DSM-5* SPD criteria compared to those without OCD. Earlier OCD onset has also been associated with co-occurring BFRBs in OCD patients [2, 16]. These findings are consistent with prior studies that found reciprocal increases of SPD rates in OCD samples and OCD rates in SPD samples, and suggests that at least part of the increased SPD prevalence seen in TS is accounted for by co-occurring OCD [18, 20]. The fact that co-occurring OCD and earlier age of OCD onset were the two most strongly associated predictors of SPD (vs. HPD) in our TS sample suggests that SPD may be more directly related to the presence of OCD than to TS (Tables 5 and S3). It will therefore be interesting to see if future studies demonstrate a closer relationship between SPD and OCD compared to HPD and OCD, especially as SPD has shown some treatment response to SSRIs (a gold-standard OCD medication) [48], whereas HPD is typically less responsive [49].

Our findings are also consistent with the hypothesis that HPD may be more closely related to tic disorders (or tic disorders with co-occurring OCD) than to OCD alone [26, 44]. Despite the previously reported association between HPD and OCD [19], we did not find significantly elevated rates of OCD in TS patients with HPD. While the small number of HPD+ patients in our sample limits the power to detect predictors of co-morbid HPD, Coffey et al. also observed that patients with TS and/or TS+OCD had higher rates of HPD than those with OCD alone, leading her to hypothesize that HPD may be a TS-spectrum disorder [26]. Additionally, Rozenman et al recently found that patients with pediatric HPD and pediatric tic disorders had more similar anxiety and depression symptom profiles compared to pediatric OCD patients [30]. The observed association between HPD and increased motor tic severity in the current study suggests that co-occurring HPD in TS patients may be indicative of a higher TS disease burden. Prior work from our group and others has also demonstrated that increased tic severity is correlated with the presence of co-morbidity in general [23, 26, 45]. However, larger samples in future studies will be needed to compare and contrast the differences between HPD and SPD and their clinical and etiological relationships to TS.

SPD in this TS sample was also associated with ADHD. Previous OCD studies have shown both ADHD and SPD to be elevated in OCD patients with tics compared to those with OCD alone [2, 26, 29]. These results parallel prior work suggesting that individuals with BFRBs have problems with impulse control, similar to findings seen in ADHD [17, 22]. Given that other clinical studies have identified impaired impulse control in patients with these disorders individually (BFRBs, ADHD, and TS [46]), one might hypothesize that TS, ADHD and BFRBs have related dysfunction in cognitive control circuitry, which might be explained by a shared genetic susceptibility. Additional research examining neurocognitive profiles and comparing imaging/genetic analyses will continue to help elucidate the comparable and contrasting factors between tics, BFRBs, impulsivity and compulsions [47]. Although this study has many strengths, including the large sample size, the use of validated, standardized diagnostic assessments, and the availability of rich clinical data, it also has limitations. First, given the small number of subjects with HPD (n=29) compared to those with SPD (n=101), there was limited statistical power to detect significant predictors in HPD + subjects, which reduced the ability to make definitive comparisons between HPD and SPD and their potential relationship(s) to TS and co-occurring conditions. Second, while this TS sample is the largest studied to date using formal diagnostic instruments [3, 25], the 3–4:1 M:F ratio led to a relative dearth of female patients. Many patients were also interviewed prior to the peak age of HPD/SPD onset, which typically occurs in early adolescence [7]; thus, some patients may not have yet developed HPD or SPD. However, this potential confound should under-estimate HPD/SPD prevalence, and we controlled for this problem to the degree possible by including age-at-assessment in the regression analyses. In addition, although we validated the BFRB questionnaire against gold-standard structured diagnostic interviews, self-reports in children/adolescents may be less accurate than those of adults. However, pediatric subjects typically completed the BFRB questionnaire with parental assistance, which in our experience improves the accuracy of responses. Because patients were recruited from major medical centers across North America, this research-based patient population may be subject to referral bias, and be more symptomatic than those in community-based samples. We know from Scharf et al [50] that rates of co-occurring OCD and ADHD in a TS population-based study tend to be lower than those found in clinical samples. Therefore, one has to be cautious about generalizing these findings to the TS population as a whole, though this study's subjects are likely more akin to TS patients one would see and assess for HPD/SPD in a clinical setting. In the future, it would be helpful to conduct similar analyses in community/non-treatment seeking samples. Another limitation is that SPD and HPD may also be associated with other clinical characteristics not assessed in our sample, including co-occurring autism spectrum, mood and/or anxiety disorders. It would be very useful to study the associations of those syndromes with HPD and SPD as well in future studies. Finally, given that our results were based on retrospective data analyses, our findings are correlational and speculative in nature, and therefore need to be tested more formally in the future.

Despite these potential limitations, this work provides important information for clinicians and researchers. Clinically, the elevated rates of HPD and SPD, particularly among females and those with OCD, suggest that these disorders should be included in routine clinical assessments of TS patients. The association of OCD and ADHD, especially with SPD in our

sample, and the early age of onset for this disorder, further suggests that these assessments should begin in early childhood, and are particularly important for children who show evidence of ADHD, as, of the three disorders, ADHD tends to have the earliest onset. In addition, the questionnaires used in this study are brief, making them feasible for use in a busy clinic, and we have demonstrated that they are valid for this population ranging from children to adults. From a research perspective, given the new diagnostic criteria and categorization schema in *DSM-5* and the recent findings of genetic overlap, it will be important to further delineate the clinical and etiological relationships of HPD, SPD and other BFRBs and TS, OCD and related disorders. Raising awareness of the co-occurrence of HPD and SPD in TS may also improve screening for these disorders and help guide patients to available treatment options and relief of suffering from these impairing conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the families, patients, and control volunteers who participated in this research, and the members of the Tourette Association for America International Genetics Consortium. This work was supported by the National Institutes of Health, grant numbers R01MH096767 (PI: Carol Mathews), U01NS040024 (PI: David Pauls/Jeremiah Scharf), K23MH085057 (PI: Jeremiah Scharf), and grants from the TLC Foundation for Body-Focused Repetitive Behaviors and from the Tourette Association of America.

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Table 1

Study sample characteristics stratified by sex (N=811)

Categorical Measures	**n (%)**	**Male (%)**	**Female (%)**	χ^2	**p-value**
Number of patients	811 (100%)	628 (77%)	183 (23%)		
OCD	422 (53%)	332 (54%)	90 (51%)	0.65	0.42
ADHD	372 (48%)	315 (53%)	57 (32%)	22.2	<0.001
Family history of TS or OCD	425 (54%)	319 (52%)	106 (59%)	2.23	0.13
Family history TS	203 (26%)	147 (24%)	56 (30%)	3.51	0.06
Family history of OCD	349 (44%)	267 (44%)	82 (45%)	0.16	0.69
Family history of HPD	52 (6.6%)	41 (6.7%)	11 (6.1%)	0.09	0.78
Continuous Measures	**Mean (SD)**	**Male Mean (SD)**	**Female Mean (SD)**	**Z**	**p-value**
TS age of onset (years)	6.1 (2.7)	6.0 (2.6)	6.5 (3.1)	1.51	0.13
OCD age of onset (years)	7.1 (3.7)	7.0 (3.7)	7.5 (3.5)	1.51	0.13
Age at interview (years)	18.8 (13.5)	18.1 (13.0)	21.3 (14.8)	3.01	0.003
YGTSS Total tic score[a] (0–50)	31.4 (8.3)	31.5 (8.2)	31.0 (8.6)	1.12	0.26
YGTSS Motor tic score[a] (0–25)	17.5 (4.3)	17.6 (4.2)	17.4 (4.3)	0.34	0.73
YGTSS Phonic tic score[a] (0–25)	13.9 (5.3)	14.0 (5.2)	13.5 (5.6)	1.39	0.17
Y-BOCS Total score[a] (0–40)	23.8 (7.2)	23.6 (7.0)	24.8 (7.8)	−1.25	0.21

TS=Tourette syndrome; OCD=obsessive-compulsive disorder; ADHD=attention-deficit/hyperactivity disorder; HPD=Hair-pulling disorder; YGTSS=Yale Global Tic Severity Scale; Y-BOCS=Yale-Brown Obsessive-Compulsive Scale; SD=standard deviation;

[a]lifetime worst-ever scores

Table 2

Univariable predictors of co-occurring Hair Pulling Disorder (HPD) in TS patients

Predictor	n (%)	OR (95% CI)	SE	z	p-value
Female Sex	11 (38)	2.21 (1.02–4.78)	0.87	2.02	0.04
OCD	19 (70)	2.16 (0.94–5.01)	0.93	1.80	0.07
ADHD	11 (46)	0.94 (0.42–2.13)	0.39	−0.14	0.89
SPD	9 (35)	3.89 (1.68–9.01)	1.67	3.18	0.001
Family history of TS or OCD	19 (70)	2.09 (0.90–4.83)	0.89	1.72	0.08
Family history of TS	8 (30)	1.25 (0.54–2.91)	0.54	0.52	0.60
Family history of OCD	16 (59)	1.88 (0.86–4.10)	0.75	1.58	0.12
Family history of HPD[b]	3 (11)	1.91 (0.55–6.59)	1.21	1.03	0.30
	Mean (SD)	**OR (95% CI)**			**p-value**
Age at interview (years)	24.5 (14.6)	1.02 (1.00–1.05)	0.01	2.21	0.03
TS age of onset (years)	5.6 (3.4)	0.92 (0.80–1.08)	0.07	−1.00	0.32
OCD age of onset (years)	6.7 (3.4)	0.96 (0.84–1.11)	0.07	−0.53	0.60
YGTSS Total score[a]	34.9 (9.1)	1.05 (1.01–1.11)	0.03	2.25	0.024
YGTSS Motor score[a]	19.9 (3.8)	1.16 (1.05–1.29)	0.06	2.87	0.004
YGTSS Phonic score[a]	15.0 (6.0)	1.05 (0.97–1.12)	0.04	1.20	0.23
Y-BOCS Total score[a]	28.8 (7.7)	1.11 (1.03–1.19)	0.04	2.84	0.005

OCD=obsessive-compulsive disorder; ADHD=attention-deficit/hyperactivity disorder; TS=Tourette syndrome; HPD=Hair Pulling Disorder; SPD=Excoriation/Skin Picking Disorder; YGTSS=Yale Global Tic Severity Scale; Y-BOCS=Yale-Brown Obsessive-Compulsive Scale; SD=standard deviation;

[a] lifetime worst-ever scores;

[b] Information on SPD family history not available.

Table 3

Multivariable predictors of co-occurring HPD in TS patients

Predictor	OR (95% CI)	SE	z	p-value
Female sex	1.97 (0.81–4.80)	0.89	1.49	0.14
Age at Interview	1.02 (0.99–1.04)	0.01	1.21	0.23
Family history of TS/OCD	1.55 (0.61–3.94)	0.74	0.91	0.36
SPD	1.92 (0.72–5.15)	0.97	1.30	0.19
OCD	1.62 (0.58–4.52)	0.85	0.92	0.36
YGTSS Motor score[a]	1.14 (1.00–1.28)	0.07	2.03	0.04

OCD=obsessive-compulsive disorder; ADHD=attention-deficit/hyperactivity disorder; TS=Tourette syndrome; HPD=Hair Pulling Disorder; SPD=Excoriation/Skin Picking Disorder; YGTSS=Yale Global Tic Severity Scale;

[a]lifetime worst-ever score; n=731, LR χ^2=17.9, p=0.006, pseudo-R^2=0.09.

Table 4

Univariable predictors of co-occurring SPD in TS patients

Predictor	n (%)	OR (95% CI)	SE	z	p-value
Female Sex	34 (34)	1.96 (1.24–3.08)	0.45	2.91	0.004
OCD	81 (81)	4.45 (2.64–7.50)	1.18	5.60	$<1.0x10^{-6}$
ADHD	60 (62)	1.91 (1.23–2.96)	0.43	2.90	0.004
HPD	9 (9.4)	3.89 (1.68–9.01)	1.67	3.18	0.001
Family history of HPD	11 (11)	2.08 (1.02–4.22)	.075	2.03	0.04
Family history of TS or OCD	68 (69)	2.13 (1.35–3.36)	0.49	3.25	0.001
Family history of TS	35 (36)	1.74 (1.11–2.73)	0.40	2.41	0.02
Family history of OCD	58 (59)	1.99 (1.30–3.07)	0.44	3.14	0.002
	Mean (SD)	**OR (95% CI)**			**p-value**
Age at Interview	19.2 (12.3)	1.00 (0.99–1.02)	0.01	0.38	0.71
TS age of onset	5.8 (2.6)	0.95 (.88–1.03)	0.04	−1.23	0.22
OCD age of onset	6.0 (2.7)	.88 (.81–.96)	0.04	−2.95	0.003
ADHD age of onset	4.0 (1.5)	.93 (.78–1.11)	0.08	−0.82	0.41
YGTSS Total score[a]	34.5 (7.8)	1.05 (1.03–1.08)	0.01	3.93	0.0001
YGTSS Motor score[a]	19.0 (3.9)	1.10 (1.05–1.17)	0.03	3.59	0.0004
YGTSS Phonic score[a]	15.5 (4.7)	1.07 (1.03–1.12)	0.02	3.30	0.001
Y-BOCS Total score[a]	25.6 (7.4)	1.05 (1.01–1.09)	0.02	2.55	0.01

OCD=obsessive-compulsive disorder; ADHD=attention-deficit/hyperactivity disorder; TS=Tourette syndrome; HPD=Hair Pulling Disorder; SPD=Excoriation/Skin Picking Disorder; YGTSS=Yale Global Tic Severity Scale;

Table 5

Multivariable predictors of co-occurring SPD in TS patients

Predictor	OR (95% CI)	SE	z	p-value
Female sex	2.08 (1.22–3.54)	0.56	2.70	0.007
OCD	4.32 (2.32–8.03)	1.37	4.63	$3.7x10^{-6}$
ADHD	1.76 (1.07–2.88)	0.44	2.24	0.025
Age at Interview	1.00 (0.98–1.02)	0.01	−0.03	0.98
YGTSS Motor score[a]	1.06 (1.001–1.13)	0.03	1.99	0.046
TS/OCD Family history	1.67 (0.997–2.79)	0.44	1.95	0.051
HPD	1.64 (0.57–4.70)	0.88	0.92	0.36

SPD=Excoriation/Skin Picking Disorder; OCD=obsessive-compulsive disorder. ADHD=attention-deficit/hyperactivity disorder; TS=Tourette syndrome; HPD=Hair Pulling Disorder; YGTSS=Yale Global Tic Severity Scale;

[a]lifetime worst-ever score; n=710, LR χ^2=67.0, p<0.00001, pseudo-R^2=0.12.