

Original Research

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Pain perception and physiological correlates in body-focused repetitive behavior disorders

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Abstract

Background. Behaviors typical of body-focused repetitive behavior disorders such as trichotillomania (TTM) and skin-picking disorder (SPD) are often associated with pleasure or relief, and with little or no physical pain, suggesting aberrant pain perception. Conclusive evidence about pain perception and correlates in these conditions is, however, lacking.

Methods. A multisite international study examined pain perception and its physiological correlates in adults with TTM ($n = 31$), SPD ($n = 24$), and healthy controls (HCs; $n = 26$). The cold pressor test was administered, and measurements of pain perception and cardiovascular parameters were taken every 15 seconds. Pain perception, latency to pain tolerance, cardiovascular parameters and associations with illness severity, and comorbid depression, as well as interaction effects (group \times time interval), were investigated across groups.

Results. There were no group differences in pain ratings over time ($P = .8$) or latency to pain tolerance ($P = .8$). Illness severity was not associated with pain ratings (all $P > .05$). In terms of diastolic blood pressure (DBP), the main effect of group was statistically significant ($P = .01$), with post hoc analyses indicating higher mean DBP in TTM (95% confidence intervals [CI], 84.0–93.5) compared to SPD (95% CI, 73.5–84.2; $P = .01$), and HCs (95% CI, 75.6–86.0; $P = .03$). Pain perception did not differ between those with and those without depression (TTM: $P = .2$, SPD: $P = .4$).

Conclusion. The study findings were mostly negative suggesting that *general* pain perception aberration is not involved in TTM and SPD. Other underlying drivers of hair-pulling and skin-picking behavior (eg, abnormal reward processing) should be investigated.

Introduction

Trichotillomania (TTM) and skin-picking disorder (SPD) are classified as body-focused repetitive behavior disorders (BFRBDs) and characterized by repetitive hair-pulling and skin-picking, respectively, with reduced control over and distress about the behavior and its sequelae.¹ The majority of individuals with TTM or SPD report little or no physical pain during pulling/picking.^{2–5} Pulling/picking episodes commonly last several hours per day, resulting in hair loss and skin damage, possibly suggesting loss of pain sensitivity.

There are several methods to determine subjective sensitivity to pain, such as focal pressure or thermal stress. Few investigations of pain perception and correlates in BFRBDs exist, however. To the best of our knowledge, there have been three empirical studies focused on this phenomenon in adults with TTM to date, all suggesting that subjective pain perception in cases is not different to that of healthy controls (HCs). In the first study, adults with TTM and HCs were exposed to a steadily increasing pressure stimulus to each fingertip of the nondominant hand, with the majority of cases failing to show hypoalgesia compared to controls.³ Similarly, in a study examining emotion regulation using self-report measures and an experimental hair-pulling task, adults with TTM and HCs reported comparable levels of physical pain after pulling out a single hair, once from a typical hair-pulling site (a site from which TTM participants usually pulled) and once from a nontypical hair-pulling site (from which TTM participants did not pull) with controls matched with TTM patients in terms of the hair-pulling sites.⁴ The third study used the

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cold pressor test (CPT), and also found no differences in pain ratings and physiological correlates of pain during immersion of the nondominant hand in ice water at a temperature ranging between 0°C and 4°C, between participants with TTM and controls.⁶

To date, there has been one empirical study in SPD that examined whether cases experience pain differently compared to HCs. Also using the CPT, this study found that adults with SPD reported similar pain tolerance (ie, the maximum amount of pain that a person can bear⁷) as controls, but exhibited a decreased autonomic response to pain as exhibited by reduced heart rate during the test compared to control participants.⁵ These findings led to the hypothesis that a “dampened” autonomic response to a pain stimulus may help explain why patients with SPD continue with a behavior that they may consciously find painful.

Notably, there are psychiatric conditions such as depression that may influence the way in which painful stimuli are perceived.^{8–10} Depression has been found to be one of the most commonly accompanying comorbidities in patients with TTM and SPD.^{11–13} The way in which such comorbidity influences pain perception in these conditions has also not been investigated.

A multisite international collaboration provided the opportunity to address these knowledge gaps and limitations of earlier pain-focused studies in TTM/SPD, providing data on pain thresholds or latency to pain tolerance, using the CPT, from the largest sample of adults with BFRBDs in which pain perception has been investigated to date. Measurements of pain perception and cardiovascular parameters (heart rate and blood pressure) taken at 15-second intervals until the pain became intolerable or until the cut-off time of 3 minutes, and the association between illness severity and latency to pain tolerance (ie, the time it takes until the pain becomes intolerable, prompting the person to demand termination of the stimulus) were compared among these cohorts. In addition, the way in which comorbid depression possibly influenced pain perception and cardiovascular variables in the patient groups were also investigated. To the best of our knowledge, this is the first study investigating pain perception and its clinical and physiological correlates in TTM and SPD simultaneously. We hypothesized that individuals with TTM or SPD will report less pain and longer latency to pain tolerance than HCs, that worse pulling/picking will be associated with lower pain ratings, that there will be objective physiological findings that are consistent with the difference in subjective pain perception between cases and controls, and that cases with comorbid depression (associated with increased pain sensitivity) will report more pain than those without such comorbidity.

Methods and Materials

Recruitment and diagnostic assessment

All participants completed a comprehensive diagnostic interview (Mini International Neuropsychiatric Interview 7.0 [MINI 7.0]), administered by a trained evaluator. Eighty-one ($n = 81$) adults, recruited from specialty clinics, the community, and the TLC Foundation for Body Focused Repetitive Behaviors (BFRBs), and meeting the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) criteria for lifetime TTM ($n = 31$) or SPD ($n = 24$) were included. The number of participants with comorbid SPD and TTM for whom we had CPT data were low ($n = 10$), resulting in the exclusion of this cohort from our analyses. In the clinical groups, comorbidity with psychiatric disorders was

allowed. Psychotropic medication was allowed except if dose changes occurred within the past 3 months. None of the participants reported any medical condition that could have interfered with their ability to take part in the study. We collected data from 26 HC volunteers, that is, individuals without current or lifetime DSM-5 psychiatric disorders, including substance abuse, or other significant medical or neurological illness and who were not currently taking any psychotropic medication. Four sites were involved in recruitment: University of Chicago, University of California, Los Angeles, Massachusetts General Hospital/Harvard Medical School, and Stellenbosch University. Recruitment started in October 2017 and ended in March 2019.

Demographic and clinical assessments

Demographic data that were collected consisted of age, gender, and level of education. Illness severity measures comprised the Clinical Global Impressions-severity scale (CGI-S), the Massachusetts General Hospital Hair-Pulling Scale (MGH-HPS), and the Skin-Picking Scale—Revised (SPS-R). The 7-item CGI-S was completed by the clinician that interviewed the participants, to assess clinical symptom severity at baseline.¹⁴ Scoring ranged from 1 (“not ill at all”) to 7 (“among the most extremely ill” patients). The self-report MGH-HPS¹⁵ was completed by participants with TTM. This is a 7-item self-report measure of pulling severity with items rated on a 0 to 4 scale (total score ranging from 0 to 28), with higher scores reflecting greater severity and increased loss of control over the behavior. The measure and its subscales have good internal consistency.¹⁶ In addition, the SPS-R¹⁷ was completed by participants with SPD. The SPS-R is a valid and reliable Likert-type self-report scale for the assessment of skin picking severity, consisting of items with scores ranging from 0 (none) to 4 (extreme). The scale yields a total score ranging from 0 to 32, with higher scores indicating greater symptom severity/impairment.

Cold pressor test

Pain perception was measured using the CPT, a reliable and valid pain induction method.¹⁸ The CPT is a cardiovascular test requiring participants to immerse their nondominant hand in ice water at a temperature ranging between 0°C and 4°C, and to withdraw their hand from the water when the stimulus becomes too painful to continue (latency to pain tolerance indication) or at the experimental endpoint of 180 seconds, whichever comes first, and measuring changes in blood pressure and heart rate over time. These changes are related to vascular response and pulse excitability. This method was used here since ice water immersion is easy to stage in the clinical setting, and perceived to be significantly more unpleasant than contact heat or electrical stimuli of equal intensity.¹⁹ Additional practical advantages and appeal of the CPT include its minimal training to use, standardization, few inherent risks, and the minimally threatening nature of cold-induced pain.²⁰ Subjective pain ratings were done on a scale from 0 (not painful at all) to 100 (extremely painful). Intermediate ratings marked on this Likert-type scale included 25 (somewhat painful), 50 (moderately painful), and 75 (very painful). Latency to pain tolerance was measured in seconds with a timer. The timer was stopped when participants reported that their hand had recovered, or no longer experienced pain. Calculation of recovery time entailed subtracting the total amount of time on the timer from the amount of time they had their hand in the water. Heart rate and blood pressure (systolic and diastolic) were recorded using an automated digital device;

heart rate at baseline and then every 15 seconds and after recovery, and blood pressure at baseline, after 30 seconds, at 180 seconds (or at the point of hand withdrawal), and after recovery.

Data analysis

Demographic characteristics and clinical features, including comorbidity and illness severity, were compared between the diagnostic groups, using chi square (χ^2) or one-way analysis of variance (ANOVA), as appropriate. For serial CPT measures, that is, measures at different time intervals, we did a repeated-measures ANOVA (RMANOVA) for each outcome measure, using a mixed model approach (including a restricted maximum likelihood test or REML). Where CPT data were not available for a participant at a given time interval due to attrition (eg, when pain could no longer be tolerated), the relevant group mean was entered into the model. The following factors were included as variables in the analyses: group (ie, TTM, SPD, or HC), time (from baseline [0 seconds], 15-second intervals, until reaching 180 seconds, and once after recovery), and the pain and physiological measurements. ANOVA was also used to investigate whether pain perception differed between patients with and those without depression.

All data were analyzed using Statistica 9.0 for Windows (Statsoft, Tulsa, OK). A 5% threshold was used as the guideline for determining significant differences. Effects' sizes of findings are included where relevant.

Ethics

The study protocol and patient information and consent forms were approved by the institutional Review Boards of all participating sites. Written informed consent was obtained from all participants prior to study procedures being conducted. Given the nature of the CPT, with its potential to cause physical or psychological discomfort, participants were free to discontinue the test at any point.

Results

Sociodemographic and clinical characteristics

The sociodemographic and clinical characteristics of study participants are depicted in Table 1. The majority of participants were female (28 of 31 TTM only, 22 of 24 SPD only, and 21 of 26 HC), with ages ranging from 18 to 68 years. The number of participants with both TTM and SPD for whom we had CPT data were low ($N = 10$), resulting in the exclusion of this cohort from our analyses. Most participants completed high school successfully, and have attained a technical school diploma, college, or university degree). There were no significant group differences in terms of the sociodemographic features (gender, age, and level of education).

Participants with BFRBDs had similar illness severity ratings, with mean CGI-S scores suggesting moderate illness severity in both patient groups (Table 1). The mean MGH-HPS total score in the TTM group was 14.8 (standard deviation [SD] 4.7), ranging from 2 to 22. In participants with SPD, the mean SPS-R total score was 16.7 (SD 5.8), ranging between 6 and 29. Seven patients with TTM (7 out of 29, ie, 24%) and two with SPD (2 out of 24, ie, 8.3%) reported "ever" receiving psychotropic medication for hair-pulling or skin-picking symptoms, respectively ($\chi^2 = 0.4$, $P = .5$). A larger number of patients with TTM had received psychotherapy over

their lifetime (44.8%), compared to patients with SPD (4.2%; $\chi^2 = 11.2$, $P = .001$, Cramer's V [CV] effect size: 0.5, moderate).

Lifetime comorbidity patterns were similar between groups, except for depression ($\chi^2 = 3.2$, $P = .08$, CV effect size: weak), body dysmorphic disorder ($\chi^2 = 3.5$, $P = .06$, CV effect size: moderate), and binge-eating disorder ($\chi^2 = 3.6$, $P = .06$, CV effect size: moderate), which tended to be more prevalent in individuals with SPD compared to those with TTM only. None of the participants reported any medical condition that could have interfered with the current study participation. Patient groups differed however in terms of a history of streptococcal infection ($\chi^2 = 8.1$, $P = .004$, CV effect size: 0.4, moderate), asthma ($\chi^2 = 4.6$, $P = .03$, CV effect size: 0.3, moderate), and headaches ($\chi^2 = 10.5$, $P = .001$, CV effect size: 0.5, moderate), with higher rates of each of these conditions in patients with SPD compared to patients with TTM.

CPT results

The 180 seconds time limit was achieved by 12 individuals with TTM (38.7%), 12 with SPD (50%), and 10 HCs (38.5%). The three groups did not differ in terms of the latency to pain tolerance, that is, the mean time period in seconds that they were able to tolerate the cold water before withdrawing ($F(2, 77) = 0.2$, $P = .8$; Cohen's d effect sizes: negligible to small) (Table 2).

There were no significant correlations between illness severity (on the CGI-S and the self-report MGH-HPS [in TTM] and SPS-R [in SPD], respectively) and pain ratings (subjective ratings, on a scale of 1-100) in any of the groups at any of the time intervals (all $P > .05$; data not shown).

The findings from the RMANOVA, including the measurements of pain, and physiological measurements (heart rate, systolic and diastolic blood pressure) were as follow (for a tabularized summary, see Supplementary Table S1):

CPT pain ratings

There were no main effects of diagnostic group in terms of subjective pain ratings ($F(2,80) = 0.01$, $P = 1.0$). A main effect of time interval ($F(11,468) = 42.9$, $P < .01$) was noted, with the pain ratings at the first five time points (from 15- to 90-second intervals) differing from one another and from the rest, as pain ratings increased significantly over these time intervals, and then plateauing from 90 seconds onwards. No statistically significant group \times time interval interaction were found for the analyses of the subjective pain ratings ($F(22,468) = 0.7$, $P = .8$; Supplementary Figure S1). In other words, alterations in pain levels over time were similar across groups.

CPT cardiovascular findings

In terms of heart rate, there was no significant main effect of diagnostic group ($F(2,80) = 0.6$, $P = .6$). The main effect of time was statistically significant ($F(13,585) = 13.6$, $P < .01$). Heart rate increased significantly until the 15-second time interval, and then gradually decreased until the 120-second interval, and then plateaued until 180 seconds, but still maintaining at a significantly higher rate compared to the start (0 seconds, or baseline; LS mean: 71.0; SE: 1.5; 95% CI, 68.0-74.0; Cohen's d : medium). After recovery, the heart rate dropped to a similar level as at baseline (LS mean: 71.0; SE: 1.5; 95% CI, 68.0-74.0; $P = 1.0$). No statistically significant group \times time interval interaction were found for the analyses of heart rate ($F(26,585) = 0.7$, $P = .8$; Supplementary Figure S2).

Table 1. Sociodemographic and Clinical Characteristics of the Diagnostic Groups

Variable	Primary Diagnosis			Statistic
	Trichotillo-mania (n = 31)	Skin-Picking Disorder (n = 24)	Healthy Controls (n = 26)	
Mean age ± SD (y)	30.8 ± 9.2	32.6 ± 13.6	28.4 ± 10.7	$F = 0.9, P = .4$
Gender ^a	Male	2	5	$\chi^2 = 2.5, P = .3$
	Female	28	21	
Level of education (n, %) ^b	High school diploma	3	1	$\chi^2 = 0.9, P = .6$
	Technical school, college or university diploma or degree	23	23	
Illness severity	Total CGI-S score (mean ± SD)	4.2 ± 0.7	4.4 ± 0.5	TTM vs SPD: $t = -1.0, P = .3$
	Total MGH-HPS score (mean ± SD)	14.8 ± 4.7	-	
	Total SPS-R score (mean ± SD)	-	16.7 ± 5.8	
Comorbidity ^c				
Major depressive disorder	7 (25.9%)	12 (50%)	-	$\chi^2 = 3.2, P = .08$
Bipolar disorder	0	0	-	-
Generalized anxiety disorder	6 (22.2%)	8 (33.3%)	-	$\chi^2 = 0.8, P = .4$
Specific phobia	0	2 (8.3%)	-	$\chi^2 = 2.3, P = .1$
Social anxiety disorder	0	1 (4.2%)	-	$\chi^2 = 1.1, P = .3$
Panic disorder	1 (3.7%)	1 (4.2%)	-	$\chi^2 = 0.01, P = .9$
Agoraphobia	0	0	-	-
obsessive-compulsive disorder (OCD)	1 (3.7%)	3 (12.5%)	-	$\chi^2 = 1.4, P = .2$
Body dysmorphic disorder	0	3 (12.5%)	-	$\chi^2 = 3.5, P = .06$
posttraumatic stress disorder (PTSD)	1 (3.7%)	3 (12.5%)	-	$\chi^2 = 1.4, P = .2$
Attention deficit hyperactivity disorder (ADHD)	1 (3.7%)	2 (8.3%)	-	$\chi^2 = 0.5, P = .5$
Anorexia nervosa	0	2 (8.3%)	-	$\chi^2 = 2.4, P = .1$
Bulimia nervosa	0	1 (4.2%)	-	$\chi^2 = 1.1, P = .3$
Binge-eating disorder	0	3 (12.5%)	-	$\chi^2 = 3.6, P = .06$
Alcohol use disorder	1 (3.7%)	0	-	$\chi^2 = 0.9, P = .3$
Substance use disorder	0	1 (4.2%)	-	$\chi^2 = 1.1, P = .3$
Medical history				
Streptococcal infection	8 (27.6%)	16 (66.7%)	-	$\chi^2 = 8.1, P = .004$
Asthma	2 (6.9%)	7 (29.2%)	-	$\chi^2 = 4.6, P = .03$
Headaches	1 (3.4%)	9 (39.1%)	-	$\chi^2 = 10.5, P = .001$
Stomachache	4 (14.3%)	6 (25%)	-	$\chi^2 = 1.0, P = .3$
Scarlet fever	0	1 (4.2%)	-	$\chi^2 = 1.2, P = .3$
Seizures	1 (3.4%)	0	-	$\chi^2 = 0.8, P = .4$
Allergies	9 (31%)	11 (45.8%)	-	$\chi^2 = 1.2, P = .3$

Values of $P < .05$ are presented in bold type.

Abbreviations: CGI-S, Clinical Global Impressions-severity scale; MGH-HPS, Massachusetts General Hospital Hair-Pulling Scale; SPS-R, Skin-Picking Severity Scale—Revised.

^aGender information of one participant (TTM) was unavailable for analysis.

^bEducation level information was unavailable for eight participants (five with TTM, one with SPD, and two healthy controls).

^cTTM vs SPD.

In terms of systolic blood pressure, there was no significant main effect of group ($F(2,78) = 1.8, P = .2$). The main effect of time was statistically significant however ($F(3,218) = 43.8, P < .01$), with post hoc tests using a Fisher LSD correction revealing significantly lower systolic blood pressure at baseline (0 seconds; LS mean: 121; SE: 2.2; 95% CI, 117.3-126.1) compared to measurements at

30 seconds (LS mean: 134.4; SE: 2.3; 95% CI, 129.8-138.9; Cohen's d : medium) and at 180 seconds (LS mean: 132.2; SE: 2.3; 95% CI, 127.7-136.7; Cohen's d : medium), and lower systolic blood pressure after recovery (LS mean: 120.2; SE: 2.2; 95% CI, 115.7-124.6; Cohen's d : negligible) compared to the measurements at 30 seconds (Cohen's d : medium) and 180 seconds (Cohen's d : medium). There

was no statistically significant group \times time interval interaction ($F(6,218) = 0.4, P = .9$; Supplementary Figure S3).

In terms of diastolic blood pressure, the main effect of group was statistically significant ($F(2,78) = 4.5, P = .01$; Figure 1), with post hoc analyses suggesting higher mean diastolic blood pressure in individuals with TTM (LS mean: 88.7; SE: 2.4; 95% CI, 84.0-93.5) compared to those with SPD (LS mean: 78.8; SE: 2.7; 95% CI, 73.5-84.2 $P = .01$; Cohen's d : medium) and HCs (LS mean: 80.8; SE: 2.6; 95% CI, 75.6-86.0, $P = .03$; Cohen's d : medium), respectively.

The main effect of time was also significant for diastolic blood pressure ($F(3,218) = 44.8, P < .01$), following the same pattern as that of systolic blood pressure, with post hoc tests revealing significant differences between measurements at baseline (0 seconds; LS mean: 78.3; SE: 1.7; 95% CI, 75.0-81.6), compared to 30 seconds (LS mean: 90.1; SE: 1.7; 95% CI, 86.7-93.5; Cohen's d : large) and

180 seconds (LS mean: 86.3; SE: 1.7; 95% CI, 83.0-89.7; Cohen's d : medium), and between measurement after recovery (LS mean: 76.4; SE: 1.7; 95% CI, 73.1-79.7) and the measurements at 30 (Cohen's d : large) and 180 seconds (Cohen's d : medium), respectively. There were no significant group \times time interval interactions ($F(6,218) = 1.1, P = .4$) for diastolic blood pressure (Supplementary Figure S4).

CPT pain ratings and comorbid depression

Within-group comparisons suggested that pain perception also did not differ between those with and those without lifetime depression (TTM: $P = .2$, SPD: $P = .4$; detail not shown).

Discussion

In this study, mostly in contrast to our hypotheses, the main findings were that (a) patient groups and controls did not differ in terms of subjective pain ratings over time and latency to pain tolerance; (b) illness severity was not associated with subjective pain ratings in any of the patient groups; (c) there were no significant group by time effects in terms of pain and any of the physiological measurements except for a significant group effect in terms of diastolic blood pressure, with post hoc analyses indicating higher mean diastolic blood pressure in TTM compared to SPD and HCs, respectively; and (d) *within-group* comparisons suggested that pain perception did not differ between those with and those without lifetime depression.

Diagnostic groups did not differ in terms of latency to pain tolerance, that is, the participants, irrespective of their diagnosis, were able to tolerate the cold water for a comparable time period

Table 2. Latency to Pain Tolerance: Mean and Range of Duration of Immersion in Ice Water (in seconds), Before Withdrawal, Across Diagnostic Groups ($P > .05$)

Group	Least Square (LS) Mean, Standard Deviation (SD) (in s)	Standard Error [SE], 95% Confidence Interval [CI]: -95.00%, +95.00%
Trichotillomania (n = 30) ^a	111.5 (65.5) range: 15-180 s	12.0, 87.0-136.0
Skin picking disorder (n = 24)	112.5 (72.0) range: 15-180 s	14.7, 82.1-142.9
Healthy controls (n = 26)	101.0 (68.7) range: 15-180 s	13.5, 73.2-128.7

^aOne of the 31 participants with TTM had missing values, and was excluded from this analysis.

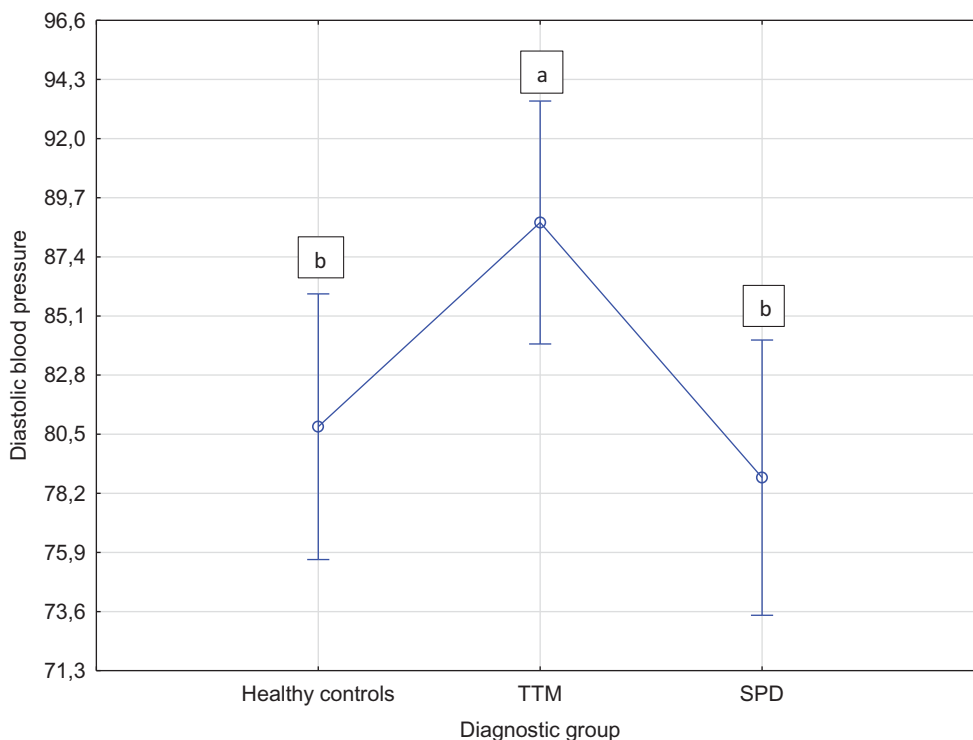


Figure 1. Mean diastolic blood pressure during the cold pressor test, across diagnostic groups ($F(2,78) = 4.5, P = .01$). ^aThe figure includes letters (a and b) to indicate post hoc differences at a 5% significance level, that is, LS means without overlapping letters are significantly different (trichotillomania [TTM] vs healthy controls [HC]: $P = .03$; TTM vs skin-picking disorder [SPD]: $P = .01$). ^bVertical bars denote 0.95 confidence intervals.

before withdrawing their hand. The different groups in our study also reported similar subjective pain ratings. This is partially consistent with previous work suggesting that subjective pain perception in cases with a BFRBD is not different to that of HCs.^{3–6} Indeed, many people occasionally engage in some skin-picking, usually without significant pain. Illness severity as measured with CGI (all participants), MGHHPs (TTM only), and SPS-R (SPD only) also did not correlate with pain ratings in any of the study groups. We did, however, find that in terms of physiological measures, patients with TTM had significantly increased mean diastolic blood pressure during the CPT compared to SPD and HCs. It is well-known that there are functional interactions between cardiovascular and pain regulatory systems, with pain generally elevating blood pressure (eg, Reference 21). A relative increase in blood pressure over time, during administration of the CPT, was thus expected in our study participants. It is not clear, however, why *diastolic* (as opposed to *systolic*) blood pressure during the CPT, in TTM (compared to the other diagnostic groups), was significantly higher. The question can be raised whether pre-existing medical conditions (or cardiovascular medications) could explain the difference in diastolic blood pressure between groups. The finding of higher rates of lifetime streptococcal infection, asthma, and headaches (conditions that may be associated with changes in blood pressure, directly or indirectly) in patients with SPD compared to patients with TTM (moderate effect sizes), is counter-intuitive and does not provide a sensible explanation for this finding. In addition, closer inspection of illness severity suggested that it was not correlated with subjective pain ratings or blood pressure measures in TTM at any time interval. More work, perhaps in larger samples, would be needed to further explore this finding of increased mean diastolic blood pressure during the CPT in patients with TTM.

The main effects of time were significant for all measures, suggesting that this pain induction method worked as intended. Specifically, in terms of mean subjective pain ratings, there was a steady increase over time until a plateau was reached at the 90-second interval, and in terms of heart rate, rates at baseline and after recovery were similar and lower than heart rate at other time intervals. Systolic and diastolic blood pressure followed comparable patterns over time, being similar at baseline and after recovery and lower than blood pressure measurements at the other time intervals.

Whether pain perception or tolerance, or autonomic responses to stimuli aimed at pain-inducement and associations with illness severity, are different in adults presenting with both TTM and SPD compared to those with either one, is not known warranting further investigation in a larger cohort. In terms of other comorbidities, individuals with BFRBDs commonly present with depression, a condition that may influence pain perception. There is evidence to suggest that increased depression symptoms lead to increased severity of perceived pain and decreased pain tolerance.²² In apparent contrast, in our sample, *within*-group comparisons suggested that subjective ratings of pain did not differ between those with and those without depression. Of note also is that the objective measures (ie, the cardiovascular parameters) did not show group differences (in the two-way or three-way interactions) when depression was present (results not shown here).

The mechanisms underlying the development and maintenance of BFRBDs are complex. Arguably, the absence of or reduced subjective pain at baseline or a pre-existing lack of an *autonomic* response to pain may constitute possible risk for developing a pathological pulling/picking compulsion,⁵ with many individuals

with TTM or SPD reporting pain or tenderness at the site of pulling *after* pulling or picking for an extended period. Reduced pain perception or lack of autonomic response may however also be the *consequence* of habituation to pain from repetitive pulling/picking or actual damage to local nociceptors.³ Such behaviors over time may *desensitize* cases to painful stimuli in terms of subjective pain levels and/or autonomic responses.⁵ In addition, our findings also suggested that *general* pain perception aberration is not involved in these two conditions. It is conceivable that individuals with TTM or SPD may have circumscribed deficiencies in pain detection in specific areas only, perhaps warranting work on *localized* pain perception. Of note, increasing pain sensitivity at the site of pulling has been proposed as a strategy for treatment in TTM. This may be particularly relevant to individuals who pull outside of awareness. It is well known that there are many individuals who automatically pull^{23–25} or pick,^{26,27} that is, completely outside of their awareness, with no urge or tension prior to, or gratification of pleasure during or after the behavior.²⁸ Arguably, increasing pain sensitivity when pulling may bring about awareness of, and perhaps consequent *aversion* to, and ultimately facilitating control or inhibition of the problematic behavior. There is theoretical and anecdotal support for the benefit of using a topical medication (eg, capsaicin cream) at the site(-s) of pulling to increase local pain sensitivity and awareness in hair-pullers who do much of their pulling outside of awareness to reduce the behavior.²⁹ There are several reasons why application of a topical cream to enhance pain sensitivity is not a practical treatment strategy though, including side-effects (when, eg, eyelids are the targeted pulling site) or given that typically a variety of picking lesions are seen, ranging from a few to hundreds, in SPD.³⁰ Increasing pain sensitivity at pulling/picking sites may thus be one (perhaps less than ideal) of several methods that may be used to increase awareness during HRT.

Considering our and other studies' negative findings, it may be argued that pain is not that important in the context of BFRBs, and that other (perhaps related) underlying drivers of hair-pulling and skin-picking behavior should rather be investigated. For example, reward processing anomalies have been implicated in BFRBDs,^{31–33} warranting further exploration. These findings seem to suggest that abnormal reward processing is a more plausible and important underlying contributor to, or reinforcer of BFRBs,^{31–33} similar to that seen in substance use disorders and other behavioral addictions, where the addictive substance or impulsive behaviors are pursued for the pleasure-generating or pain-relieving effect.^{34,35} Importantly, this reward-based model may have clinical utility; it has been proposed that an intervention aimed at decreasing brain activation in the striatum (or the reward brain network that includes the striatum) is needed to address the underlying reward processing dysregulation inherent in TTM.³⁶ Continuing the debate in the literature around reward and other plausible drivers of pulling/picking would be invaluable for future treatment developments and our understanding of what drives these BFRBs.

Study limitations include a small sample size, reducing the power of the study. Nevertheless, this is the largest sample individuals with BFRBDs to date in which pain perception and cardiovascular parameters have been investigated. The number of male participants was too low to allow examination of gender differences in terms of the investigated phenomena. This may potentially be important given that studies have showed that men and women differ significantly regarding pain perception, especially under experimental conditions.^{37,38} Of note, however, the current study included diagnostic groups that were well matched in terms of their

sociodemographic features, that is, most were female, in their 20s or 30s, and with some college/university education. Also, although a well-respected model of pain perception and one of the most used experimental pain modalities was used here, other methods of assessing response to painful stimuli, and applying pain stimuli in pulling/picking (vs nonpulling/picking) areas, for example, could theoretically yield different results. Indeed, although we did not find pain sensations to be globally altered in TTM or SPD, it may be that they are diminished only at the sites of pulling/picking rather. Moreover, it may be that the CPT involves different nociceptors (ie, the relatively unspecialized nerve cell endings that initiate the sensation of pain) than those relevant to hair-pulling or skin-picking. The use of an alternative, perhaps specifically focused pain induction method, involving mechanosensitive or polymodal nociceptors that may be relevant to TTM/SPD, and which would allow such a targeted investigation in BFRBDs, is warranted. A third limitation involves not investigating the impact of comorbidities other than depression in the respective patient groups or not including a cohort with comorbid TTM and SPD. As perception of pain may be influenced by the number of, and presence of some comorbidities such as anxiety and obsessive-compulsive disorders¹⁰ and since concomitant TTM and SPD may differ from solitary TTM and SPD in terms of comorbidity patterns, this is another avenue for further exploration, in a larger study sample. Finally, information on the use of cardiovascular medication which may have influenced findings were not collected. Respondents reporting medical conditions that could have compromised their ability to take part in this trial, including cardiovascular concerns, were excluded from taking part, however.

In conclusion, the mechanisms underlying the development and maintenance of BFRBDs are complex. Investigating pain perception in TTM and SPD further, our findings suggested that *general* pain perception aberration is not involved in these two conditions. Further work is needed on *localized* pain perception as well as other (perhaps related and/or inter-playing) processes, such as abnormal reward processing,^{31–33} implicating the positive reinforcement from pleasure-generating or relief-action endorphin systems that are involved in other overlapping conditions such as the addictions^{34,39} and impulse control disorders.³⁵

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