Optimizing psychological interventions for trichotillomania (hair-pulling disorder): an update on current empirical status

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Abstract: Trichotillomania (hair-pulling disorder) is a psychiatric condition characterized by a persistent habit of pulling out one’s hair. In treatment-seeking populations, hair-pulling disorder can be severe, chronic, and difficult to treat. In the early 1970s, behavioral interventions (eg, habit reversal training) were developed and proved effective in treating chronic hair-pulling for many individuals. In order to further increase treatment efficacy and improve long-term outcome, several authors have developed augmented treatment protocols that combine traditional behavioral strategies with other cognitive-behavioral interventions, including cognitive therapy, dialectical behavioral therapy, and acceptance and commitment therapy. In the present review, we give an overview of the clinical and diagnostic features of hair-pulling disorder, describe different cognitive-behavioral interventions, and evaluate research on their efficacy.

Keywords: trichotillomania, hair-pulling, cognitive-behavioral therapy, diagnosis, review

Introduction

Trichotillomania (hair-pulling disorder; HPD) is a psychiatric problem marked by a persistent habit of pulling out one’s hair. Although HPD has been recognized in the medical literature for more than a century, the disorder has received limited attention. It was only with the publication of the DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised) in 1987, that the condition was formally recognized as a psychiatric disorder. In the current edition of the DSM (DSM-5), HPD is defined as recurrent hair-pulling that is not better explained by a medical condition (eg, dermatological problems) or another psychiatric disorder (eg, a psychotic disorder) and causes hair loss, repeated failed attempts at stopping the behavior, and subjective distress or impairment in functioning.

HPD tends to be a chronic condition and can be difficult to treat. In the early 1970s, Azrin et al developed behavioral interventions, eg, habit reversal training (HRT), which proved effective in reducing or eliminating a variety of habit behaviors, including chronic hair-pulling. In recent years, several authors have attempted to augment traditional behavioral strategies with other cognitive-behavioral interventions, including cognitive therapy (CT), dialectical behavioral therapy (DBT), and acceptance and commitment therapy (ACT). This literature has produced some promising findings and a consensus is emerging among experts that cognitive-behavioral interventions should be regarded as the first-line treatment for HPD. However, surveys indicate that a majority of mental health providers have limited knowledge of HPD and its treatment. The objectives of this paper are to provide an overview of the clinical and diagnostic features of HPD and to evaluate research on cognitive-behavioral interventions.
features of HPD, describe different cognitive-behavioral treatment interventions, and review treatment efficacy research.

Clinical characteristics
Epidemiology and course
Surveys indicate that about 1% of the general adult population and 2%–4.4% of the general psychiatric outpatient population meet the criteria for HPD. Of those who seek treatment for HPD, a large majority (88%–94%) are female. The most common age of onset is early adolescence, although HPD can occur at any age. Onset in early childhood is frequently reported. Some authors have suggested that early onset cases (younger than 5 years) may represent a subtype of HPD that is less chronic than later-onset cases; however, this notion has yet to be empirically tested in a longitudinal study.

Symptom presentation
Individuals with HPD typically pull hairs one by one with their fingers, although some also use tweezers or other instruments. Length and number of pulling episodes vary substantially across individuals. Interviews with 70 adult HPD patients showed that the median pulling time was 45 minutes each day. Scalp, eyebrows, and eyelashes are the most common pulling sites across all age groups, but all body areas can be affected, including the pubic region, legs, and armpits. Many individuals with HPD report playing with pulled hair (e.g., stroking the hairs against the lips). Approximately 10%–30% of individuals with HPD report eating pulled hairs, often by biting off and consuming hair roots. HPD patients who ingest pulled hairs may develop trichobezoars that can lead to serious gastrointestinal complications and typically require surgery.

Impairment and distress
HPD is often associated with significant impairment and distress in emotional and social domains. Inability to control hair-pulling behavior and related changes in appearance can result in shame, embarrassment, and social avoidance. As social avoidance increases due to hair-pulling, social disability becomes more profound. Some studies have shown that the severity of HPD symptoms is not predictive of quality of life concerns, while others have found that HPD severity is associated with poor body esteem, difficulty in forming close social friendships, and compromised academic success. HPD can also have adverse financial consequences as many patients undertake costly efforts to cover affected areas (e.g., wigs, hair extensions, and clothing).

Phenomenology
Automaticity
Hair-pulling behavior can be quite automatic. Some individuals are reflectively unaware of the behavior as it occurs and realize only afterward what they have done. This automatic pulling is especially common in situations where the attention is absorbed in some other activity, such as driving a car, talking on a telephone, watching television, or reading a book. People differ in how often they pull out hairs in this automatic fashion, but it is very rare that an individual will exclusively pull automatically.

Cognition and sensory phenomena
Individuals with HPD sometimes report dysfunctional thinking or sensory phenomena that appear to play a role in hair-pulling. For example, some patients experience strong urges to pull when they notice certain types of hairs, typically hairs that are different from the rest (e.g., gray, thick, coarse, or wiry hairs). These urges are often triggered by automatic thoughts (e.g., “gray hairs must go”) or inexplicable sensory experience that things are “just not right”. The role of cognitive/sensory factors is supported by strong clinical impression, but limited empirical attention has been given to these factors in HPD.

Affective experiences
Studies show that the majority of individuals with HPD report pleasurable feelings or gratification during or after pulling out hairs. Studies have also shown that many individuals with HPD report boredom, tension, or anxiety before pulling episodes, and a significant reduction in such negative emotions following pulling. This suggests that pulling may serve to downregulate negative emotions.

Diagnostic considerations
Diagnostic features
The core diagnostic feature of HPD is the recurrent pulling of hairs from one’s own body, which results in loss of hair. In previous editions of the DSM (e.g., DSM-III-R), HPD was classified as an impulse control disorder and its diagnostic criteria required mounting tension before pulling and gratification or relief during pulling. Studies have since shown that about 10%–20% of individuals with clinically significant hair-pulling problems do not endorse these experiences, so these requirements were omitted from the DSM-5 criteria. In order to distinguish HPD from normal or non-pathological hair-pulling (e.g., non-problematic grooming practices) the DSM-5 criteria includes the traditional requirement of either
significant subjective distress or impairment in functioning due to hair-pulling behaviors. Additionally, the DSM-5 criteria requires that the individual has had repeated failed attempts at stopping or reducing the behaviors.

Differential diagnoses
In the DSM-5, HPD is classified as an obsessive-compulsive and related disorder. Research has shown that HPD and obsessive-compulsive disorder (OCD) often co-occur and aggregate in the same families. However, HPD and OCD have important differences in epidemiology (eg, sex ratio) and phenomenology. Most importantly, unlike compulsions in OCD, hair-pulling behavior in HPD is associated with pleasurable feelings and is rarely, if ever, preceded by pathological obsessions or concerns about potential harm. Some HPD patients may report a desire to obtain symmetry (eg, evening out eyebrows) or to relieve a sense of incompleteness (eg, a “just not right” feeling). However, these experiences typically do not warrant a diagnosis of OCD, and are rarely the sole reason for pulling behavior. In cases where hair-pulling is solely due to obsessions in OCD, HPD should not be diagnosed. Some HPD patients may report feeling that pulling is improving or fixing their appearance (eg, pulling out “abnormal-looking” hairs). In these cases, however, hair-pulling is typically not driven by concerns about looking ugly or abnormal. When hair-pulling is solely due to appearance concerns as in the case of body dysmorphic disorder, a diagnosis of HPD is not warranted. Hair-pulling caused by psychotic symptoms (eg, delusions of parasitosis) should not be diagnosed as HPD. Repeated hair-pulling, or bald spots resembling those produced by HPD, may be caused by dermatological or other medical conditions (eg, alopecia areata, telogen effluvium, tinea capitis, lichen planopilaris, or alopecia mucinosa). In these cases, HPD should not be diagnosed. Dermatological evaluation may help determine diagnosis in cases where the individual denies the habit, or to rule out differential diagnoses.

Cognitive-behavioral models
Different cognitive-behavioral models of HPD have been developed with overall similar emphases. These models typically assume that hair-pulling is an operant behavior shaped by reinforcing (and punishing) consequences. In addition, it is often assumed that some biological vulnerability factors may render certain individuals susceptible to experiencing strong affective reactions to hair-pulling behaviors. Consequently, for these individuals, hair-pulling behaviors readily become reinforced because they produce gratification or pleasurable feelings (positive reinforcement) or downregulate aversive experiences such as urges, tension, anxiety, or boredom (negative reinforcement).

Wetterneck and Woods proposed a similar, but more nuanced, emotion regulation model on the bases of a “third wave” behavioral theory. According to this model, the underlying problem with HPD is a general tendency to avoid or escape aversive private experiences (so-called experiential avoidance), which in turn promotes the development of hair-pulling as a coping strategy that helps avoid aversive states.

According to cognitive-behavioral therapy (CBT) models, certain thoughts (“this gray hair must go”) or sensory phenomena (eg, a “just not right” feeling after noticing a thick hair) may trigger pulling behaviors. Moreover, cognitive/sensory experiences often appear to mediate the reinforcing consequences of the behavior. For example, individuals may prefer to pull hairs with certain features (eg, wiry hair or hair with a root on the end) and experience enhanced gratification when they pull out those types of hair. Thus, CBT models would assume that cognitive/sensory experiences influence the extent to which hair-pulling is gratifying.

Finally, CBT models typically assume that over time contextual factors can acquire the ability to trigger urges to perform the behaviors, through the mechanisms of classical conditioning. For example, an individual may tend to pull hair when feeling bored or sitting in a certain chair watching television. Over time, contextual features (eg, the state of boredom, time of day, the specific room, being alone) acquire the ability to trigger the urge to pull.

Cognitive-behavioral therapies
In Table 1 we provide a brief description of cognitive-behavioral strategies that have proven useful in the treatment of HPD.

Habit reversal training/stimulus control
Overview
Azrin et al developed HRT as a multimodal behavioral therapy for tics and habit behaviors. Most researchers have used a simplified version of HRT that includes awareness training, competing response training, and social support or contingency management. In addition, HRT is typically implemented along with stimulus control (SC) interventions.

Awareness training
The goal of awareness training in HRT is to increase a patient’s awareness of his/her hair-pulling behavior. The core component is a careful functional assessment interview, in
The exercise increases the patient’s awareness of the “warning sign” or cues that predict hair-pulling behavior is about to occur. The most reliable signs tend to be early motor components in the behavior chain leading to pulling behavior (eg, moving the hand toward the pulling site). However, other physical or emotional antecedents to pulling may also serve as relatively reliable “warning signs”. In addition to a functional assessment interview, the patient is asked to engage in self-monitoring for pulling symptoms at home which further enhances awareness of the behavior and its context.

Once antecedents or “warning signs” have been identified, awareness training may also involve in-session exercises. In these exercises, the patient and therapist engage in casual conversation during which the patient is asked to indicate (by lifting a finger) when he/she notices a “warning sign” or actual pulling behavior. The exercise increases the patient’s awareness of the “warning sign” and helps clearly define what the “warning sign” is and is not.

### Competing response training

In competing response training, the patient is trained to perform a specific action (a competing response) every time he or she notices a “warning sign” or actual pulling behavior. The competing response should be selected in collaboration with the patient, and should be inconspicuous, easy to perform, and physically incompatible with the pulling behavior (ie, it should be impossible to pull at the same time). Common competing responses include making hands into a fist, sitting on hands, and putting hands in pockets. The patient is instructed to perform the competing response for 1 minute, or until the urge has subsided (whichever is longer), contingent on “warning sign” or pulling behavior.

### Social support training/contingency management

The goal of social support training is to train a “support person” in the patient’s environment to reinforce and praise successful use of competing responses. The role of the support person is twofold: he/she reinforces the patient’s
correct performance of competing responses and helps increase awareness by pointing out “warning signs”. Because the goal is to facilitate competing responses, the support person must be trained in how to point out “warning signs” in an uncritical manner with encouragement. To this end, the support person may be asked to join therapy sessions (especially if the support person is the parent of a patient in pediatric treatment).

Stimulus control
The goal of SC interventions is to minimize the influence of environmental factors on pulling behavior. After a careful functional assessment of antecedents and consequences of pulling behavior, the patient and therapist design interventions that eliminate triggering cues, and make pulling behavior more effortful or less rewarding. These interventions may involve discarding tweezers, covering bathroom mirrors, restricting time in high-risk situations (eg, reduce time using the bathroom), sitting in different chairs (eliminate postural cues), pre-emptively reducing the effects of certain emotional states (eg, avoid situations of being alone and bored) and making pulling behavior more difficult to perform (eg, wearing gloves or putting on fake nails).

Enhancement strategies
Overview
In recent years, clinicians and researchers are increasingly relying on enhanced behavior therapy protocols that combine HRT/SC with strategies directed at internal states (eg, urges or negative emotions) that play a role in HPD. These strategies include CT, DBT, and ACT.

Cognitive therapy
The aim of CT is to modify dysfunctional cognitive tendencies that may play a role in HPD. Common problematic cognitions in HPD include dysfunctional beliefs about certain hair types (“gray hairs must go”), “slippery slope” thinking (“I will only pull one hair and then stop”), and justifications (“I have had a bad day, so I deserve to pull”). Through in-session exercises/discussions and homework assignments (eg, thought records) the therapist teaches the patient to identify dysfunctional cognitions and emotions that occur before, during, and after pulling episodes, and appreciate their role in the habit. The patient is then helped to evaluate evidence for and against problematic cognitions and consider more adaptive alternatives. For example, it can be very helpful to realize that certain automatic thoughts prolong pulling episodes (“I need to find a hair with a root on it”). Such thoughts can then be evaluated in terms of usefulness and validity, and a more appropriate way of thinking can be introduced.

Dialectical behavior therapy
Keuthen et al developed a 15-session treatment protocol that emphasizes HRT/SC and DBT. The aim of the DBT component is to address emotion regulation difficulties that are assumed to underlie the development and maintenance of HPD. Specifically, DBT seeks to enhance awareness of affective states such as anger, boredom, and frustration, address maladaptive emotional regulation strategies that may cue, reinforce, and maintain hair-pulling, and replace them with more adaptive emotion regulation skills. DBT for HPD has two core components. First, DBT incorporates mindfulness exercises to enhance awareness of pulling urges and behavioral antecedents. These mindfulness exercises also function to decrease reactivity to emotional cues. Second, DBT provides emotion regulation skills (eg, distress tolerance training) to address the impact of negative affective states on hair-pulling. Within this skill, a therapist may teach the patient progressive muscle relaxation and acceptance-based strategies, as well as distraction strategies (ie, engaging in a hobby), soothing strategies, and “improving the moment” strategies (ie, visualizing tranquility).

Acceptance and commitment therapy
Woods et al developed a ten-session treatment protocol (usually implemented over a 12-week period) that combines HRT/SC and ACT. The ACT component is based on the assumption that hair-pulling behavior originates from experiential avoidance, ie, an unwillingness to experience certain aversive states and a tendency to avoid or escape them. It is assumed that experiential avoidance makes individuals with HPD attempt to avoid or escape urges, negative emotions, or other aversive experiences by pulling hairs.

In brief, ACT aims to help the patient to develop a new outlook where their actions are not controlled by aversive internal experiences, but guided by valued life goals. The first step is to help the patient clarify what his or her core values and life goals are. The patient is then taught to realize how the struggle with pulling urges (and other aversive experiences) has interfered with these goals and failed to successfully reduce pulling behaviors. ACT also emphasizes that having urges to pull is not problematic in itself; and that reacting to urges by pulling is the problem. The patient is then asked to consider the benefits of stop struggling with internal experiences, and instead willingly accept them. At the same time, the patient is encouraged to commit to letting
core values and life goals, not aversive internal experiences, guide behavior. These issues are explored through in-session exercises, demonstrations, discussions, metaphors, and homework assignments.

Other strategies in CBT protocols

In addition to the techniques described above, CBT protocols often include other components such as psychoeducation, motivational enhancement, relaxation training, and relapse prevention. Motivational enhancement may involve simple inconvenience review (eg, listing pros and cons associated with the habit), or more extensive motivational interviewing techniques. The most common relaxation techniques include diaphragmatic breathing exercises and progressive muscle relaxation. Relapse prevention often emphasizes the identification of potential high-risk situations or triggering events and the development of appropriate coping strategies.

Treatment efficacy research

Habit reversal training/stimulus control

Evidence suggests that HRT/SC is effective in the treatment of HPD. van Minnen et al randomized 43 adults with HPD to either six sessions of HRT/SC (conducted bi-weekly), 12 weeks of fluoxetine treatment, or a 12-week waiting list condition. Clinician ratings post treatment indicated that 64% of the HRT/SC group had shown “much” or “very much” improvement. Only 9% of the fluoxetine group and 20% of the waiting list had attained this level of improvement. However, a follow-up study of subjects in the HRT/SC condition indicated a significant increase in symptoms for many participants at 2-year follow-up. Complete abstinence from hair-pulling and low levels of depression post treatment predicted maintenance of therapeutic gain at follow-up.

Self-help versions of HRT/SC may also be beneficial for patients with HPD. Mouton-Odum et al examined the efficacy of an interactive online self-help program based on HRT/SC (stopPulling.com; monthly fee 30 USD). Naturalistic data from 263 consecutive users indicated moderate treatment efficacy. At post treatment, 32% of participants had obtained at least a 25% reduction in symptom severity (assessed with a validated self-report questionnaire, ie, the Massachusetts General Hospital Hair-pulling Scale).

More recently, Rogers et al investigated a stepped care approach in the treatment of HPD. In step one, 60 adults with HPD were randomized to either a 10-week self-help treatment using the stopPulling.com condition (free of charge) or a 10-week waiting list condition (before completing the self-help program). The stopPulling.com condition produced a small but significant treatment effect (d=0.21) according to clinician ratings. In step two, 76% of participants self-selected into an additional eight-session HRT/SC treatment with a therapist (those with greater post treatment symptom severity were more likely enroll in step two). Half of the participants in step two showed clinically significant improvement post-treatment. For example, while 97% met DSM-IV criteria for HPD during enrollment, only 45% met the criteria post treatment. A 3-month follow-up indicated moderate maintenance of treatment gains. Complete abstinence post treatment and lower symptom severity during the initial response predicted greater maintenance of treatment gains at follow-up.

Enhancement with cognitive therapy

Franklin et al examined the efficacy of an eight-session treatment protocol that consisted of HRT/SC, relaxation training, and cognitive restructuring. Twenty-four youths (aged 7–17 years) with HPD were randomized to a CBT protocol or a minimal attention waiting list condition. Post treatment clinician-ratings showed that 75% of the youths in the CBT condition and 0% in the control condition were considered “much” or “very much” improved. The results also showed overall good maintenance of treatment gains at 2-month follow-up.

Similar findings have been obtained in adult HPD samples. Lerner et al examined the efficacy of a 9-week CBT protocol (HRT/SC, CT, and relaxation training) in an uncontrolled trial. Results showed that 12 (85%) of the 15 participants had significant improvement post treatment (ie, more than 50% reduction in clinician-rated symptom severity). Ninan et al conducted a small randomized trial where adults with HPD were assigned to either a nine-session CBT protocol (n=5) that included HRT/SC, stress management, and cognitive therapy, 9 weeks of treatment with clomipramine (n=6), or a 9-week placebo pill condition (n=5). Clinician ratings post treatment indicated that all five participants in the CBT condition (100%), four of six in the clomipramine condition (67%), and no one in the placebo pill condition (0%), were “much” or “very much” improved.

Diefenbach et al evaluated the efficacy of a similar CBT protocol implemented in a group format. In a randomized trial, a 12-week group CBT condition (n=12) was compared with a 12-week group social support condition (n=12). The results showed significantly greater symptom reduction in the CBT group compared with the social support group. After treatment, eight participants (67%) in the CBT group and three...
(25%) in the support group were considered “much” or “very much” improved. At 6-month follow-up, four (33%) in the CBT group and three (25%) in the social support group had maintained this level of improvement. These findings suggest that although group CBT may be helpful for many patients, the treatment is more likely to yield long-term therapeutic effects when conducted in individual therapy compared with a group format. Toledo et al. randomized 44 HPD patients to 22 sessions of supportive group therapy versus CBT group therapy. Non-blind evaluation post treatment showed that 90% of patients in the CBT group were classified as “much” or “very much improved” compared with 59% in the supportive therapy group. The overall greater response rate in this study suggests a potential therapeutic benefit of increasing the number of treatment sessions in the group therapy for HPD.

Enhancement with dialectical behavioral therapy

Evidence indicates that DBT-enhanced HRT/SC can be an effective treatment for HPD. Case studies have shown that DBT-enhanced HRT/SC significantly reduces symptoms among adults and adolescents with HPD. Keuthen et al. examined the efficacy of DBT-enhanced HRT/SC in the treatment of ten adults with HPD. The treatment included eleven weekly therapy sessions and four booster sessions over 3 months. Clinician ratings indicated that eight of the ten participants (80%) were considered “much” or “very much” improved after the acute treatment phase, and all participants maintained their gains through the booster session phase. Further, 6-month follow-up showed good maintenance of treatment gains. Using the same treatment protocol, the investigators conducted a randomized controlled trial where DBT-enhanced HRT/SC (n=20) was compared with minimal attention control (n=18). Post treatment, eleven of the 20 (55%) participants in the treatment condition were considered “much” or “very much” improved. Only one participant (5.5%) in the minimal attention control condition demonstrated such improvement. Again, the treatment gains were largely maintained at 6-month follow-up. Reduction in symptoms was correlated with increased emotion regulation capacity, which is consistent with the notion that increased emotion regulation skills serve as a mechanism of action in the treatment.

Enhancement with acceptance and commitment therapy

Case studies have shown that ACT-enhanced HRT/SC is effective in reducing HPD symptoms in adults and adolescents. Further, Woods et al. conducted a controlled trial where 25 adults with HPD were randomized to either a ten-session ACT-enhanced HRT/SC protocol or a waiting list. Self-reports and independent clinician ratings showed significantly greater HPD symptom reduction in the treatment condition compared with the wait list condition. Post treatment, 66% of participants in the treatment condition and 8% in the waiting list condition were considered treatment responders according to self-reported HPD severity/imairpment. Treatment gains were generally maintained at 3-month follow-up. Reduction in self-reported experiential avoidance was correlated with change in symptoms, suggesting that greater acceptance of aversive internal states (eg, urges) mediates the treatment effects. Greater treatment compliance was also found to predict a favorable outcome.

Conclusion

Research has consistently shown that at least 50%-60% of individuals with HPD derive clinically meaningful benefits from psychotherapy that involves HRT/SC. Meta-analyses that pool results from existing trials have also confirmed the efficacy of HRT/SC. Self-help programs and group therapy based on HRT/SC may also be beneficial for some individuals with HPD. However, in-person individual therapy appears to be the optimal form of treatment. Preliminary data suggest that a greater number of therapy hours, in group or individual therapy, may be associated with a better outcome.

Despite strong evidence for the efficacy of HRT/SC, many patients show only limited improvement, and those who gain benefits often relapse after treatment. In an effort to address these limitations, several researchers have attempted to augment HRT/SC with treatment components that focus on internal experiences, such as urges and negative affect. Studies have shown that augmenting HRT/SC with CT, DBT, or ACT may be beneficial to patients, and results have generally shown favorable maintenance of therapeutic gains over 3–6 months of follow-up. However, no study has examined relapse rates beyond 6 months. It should also be noted that the incremental efficacy of these treatment components has not been tested directly. No study has compared the efficacy of HRT/SC with that of HRT/SC plus CT, DBT, or ACT, and no controlled trials have examined the efficacy of CT, DBT, or ACT as monotherapies (ie, without HRT/SC). Nevertheless, clinical impression and psychopathology research suggest that urges, impulses, cognitions, and affective experiences play an important role in hair-pulling episodes. It therefore seems reasonable to assume that addressing such experiences in treatment may be beneficial and contribute to the efficacy of HRT/SC. Also, a meta-
analysis showed a significantly larger effect size in treatment trials involving augmented protocols when compared with HRT/SC alone. Finally, existing data suggest that the efficacy of augmented treatment protocols is at least partly mediated by an increase in a patient’s ability to regulate or accept aversive internal experiences.

Do some treatment components fit better with certain type of patients? It has been hypothesized that CT, DBT, and ACT are mostly efficacious for individuals with “focused” pulling styles, ie, individuals who tend to pull in response to private events, such as urges, negative emotions, or “just not right” experiences. In turn, it is argued that individuals with an “automatic” pulling style, ie, those who pull without reflective awareness, may benefit less from these strategies, and more from HRT/SC, given its emphasis on awareness training and environmental triggers. However, a majority of those with HPD report both automatic and focused pulling styles, and one cannot rule out that automatic pulling also serves to regulate emotions. It is therefore likely that most individuals with HPD will benefit from augmented treatment protocols.

Disclosure
The authors report no conflicts of interest in this work.

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