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Treating trichotillomania: A meta-analysis of treatment effects and moderators for behavior therapy and serotonin reuptake inhibitors

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ABSTRACT

Few randomized controlled trials (RCTs) exist examining the efficacy of behavior therapy (BT) or serotonin reuptake inhibitors (SRIs) for the treatment of trichotillomania (TTM), with no examination of treatment moderators. The present meta-analysis synthesized the treatment effect sizes (ES) of BT and SRI relative to comparison conditions, and examined moderators of treatment. A comprehensive literature search identified 11 RCTs that met inclusion criteria. Clinical characteristics (e.g., age, comorbidity, therapeutic contact hours), outcome measures, treatment subtypes (e.g., SRI subtype, BT subtype), and ES data were extracted. The standardized mean difference of change in hair pulling severity was the outcome measure. A random effects meta-analysis found a large pooled ES for BT (ES = 1.41, $p < 0.001$). BT trials with greater therapeutic contact hours exhibited larger ES ($p = 0.009$). Additionally, BT trials that used mood enhanced therapeutic techniques exhibited greater ES relative to trials including only traditional BT components ($p = 0.004$). For SRI trials, a random effects meta-analysis identified a moderate pooled ES (ES = 0.41, $p = 0.02$). Although clomipramine exhibited larger ES relative to selective serotonin reuptake inhibitors, the difference was not statistically significant. Publication bias was not identified for either treatment. BT yields large treatment effects for TTM, with further examination needed to disentangle confounded treatment moderators. SRI trials exhibited a moderate pooled ES, with no treatment moderators identified. Sensitivity analyses highlighted the need for further RCTs of SRIs, especially among youth with TTM.

1. Introduction

Hair pulling behaviors are common in the general population (Duke et al., 2009), with between 1% and 3% of adults reporting clinically significant hair pulling (Christenson et al., 1991b). Hair pulling disorder, commonly referred to as trichotillomania (TTM), is characterized by excessive hair pulling that can be automatic (e.g., outside of awareness) or focused (e.g., consciously pulled) in nature (American Psychiatric Association, 2013; Stein et al., 2010). Individuals with TTM frequently experience co-occurring anxiety disorders, depressive disorders, and other body-focused repetitive behaviors (Duke et al., 2010; Panza et al., 2013). Hair pulling behaviors can result in detrimental physical complications (Bouwer and Stein, 1998), psychosocial impairment (Diefenbach et al., 2005b; Stemberger et al., 2000; Wetterneck et al., 2006; Woods et al., 2006a), and poor quality of life (Diefenbach et al., 2005b; Odlaug et al., 2010). In light of these deleterious physical and psychological consequences, effective and efficient treatments are needed.

Several therapeutic approaches have been investigated to treat TTM symptoms (Franklin et al., 2011b), including behavior therapy (BT) and psychiatric medications (Franklin et al., 2008; Woods et al., 2006a). Behavioral therapies such as habit reversal training (HRT) have demonstrated efficacy reducing hair pulling severity across several randomized controlled trials (RCTs) (Azrin et al., 1980; Diefenbach et al., 2006; Franklin et al., 2011a; Ninan et al., 2000;

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van Minnen et al., 2003), with more recent BT trials including components of acceptance and commitment therapy (ACT) (Woods et al., 2006b), and dialectical behavior therapy (DBT) (Keuthen et al., 2012). Acute treatment gains obtained from BT have been generally maintained up to six months (Franklin et al., 2011a; Keuthen et al., 2011; Woods et al., 2006b). Indeed, BT is recommended as a first-line treatment for youth and adults with TTM (Flessner et al., 2010). Despite noted efficacy, RCTs of BT have had relatively small sample sizes, with no examination of treatment moderators.

Aside from BT, two types of psychiatric medications (antipsychotics and antidepressants) have demonstrated mixed efficacy in reducing hair pulling. While antipsychotic medications (e.g., olanzapine, aripiprazole) have demonstrated efficacy in open-label trials (Stewart and Nejtek, 2003; White and Koran, 2011), only one RCT has evaluated the efficacy of olanzapine and identified its therapeutic benefit relative to placebo (Van Ameringen et al., 2010). Comparatively, antidepressant medications (e.g., clomipramine, fluoxetine, sertraline) remain the most frequently used treatment for individuals with TTM (Franklin et al., 2008; Woods et al., 2006a), but have mixed evidence across RCTs (Christenson et al., 1991a; Dougherty et al., 2006; Ninan et al., 2000; Streichenwein and Thornby, 1995; Swedo et al., 1989; van Minnen et al., 2003), with some evidence of long-term therapeutic benefit (Swedo et al., 1993). These medications share the commonality of inhibiting the reuptake of serotonin (referred to as serotonin reuptake inhibitors, SRIs) leading to the belief that deficiencies of serotonin may underlie hair pulling behaviors (Ferrão et al., 2009; Mancini et al., 2009). Despite mixed efficacy, side effect profiles, and potential high relapse rates following discontinuation (Iancu et al., 1996; Pollard et al., 1991); SRI medications are frequently used (Franklin et al., 2008; Woods et al., 2006a) and recommended by experts as pharmacological treatment options (Chamberlain et al., 2007).

More recently, *N*-acetylcysteine (i.e., an over-the-counter amino acid supplement that acts as a glutamate modulator; NAC) has been evaluated in the treatment of individuals with TTM. While demonstrating efficacy in an RCT of adults with TTM (Grant et al., 2009), no significant benefit was found relative to placebo in a sample of youth with TTM (Bloch et al., 2013). Although offering promise for some individuals (Woods, 2013), the small number of RCTs limits inferences about NAC's efficacy for TTM.

When making treatment recommendations, it is important to synthesize empirical evidence to guide clinical decisions (Murad and Montori, 2013). Relative to literature reviews and expert recommendations, meta-analyses provide a quantitative synthesis of treatment trials, and allow for the examination of moderators of treatment effects. Presently, only one meta-analysis has examined the efficacy of behavioral and pharmacological treatments for reducing hair pulling behaviors among individuals with TTM (Bloch et al., 2007). Bloch et al. (2007) found a large treatment effect for HRT [Standardized Mean Difference (SMD) = 1.14, 95% Confidence Interval (CI): −1.89, −0.38] compared to control conditions. Clomipramine (CMI) was found to be superior to comparison conditions (SMD = 0.68, 95% CI: −1.28, −0.07), with no significant effect found for selective serotonin reuptake inhibitor medications (SSRIs) relative to placebo (SMD = 0.02, 95% CI: −0.32, 0.35). While beneficial as the first quantitative synthesis of this area, this meta-analysis has several limitations in the present-day context (Bloch et al., 2007). First, since its publication, several additional RCTs of BT for TTM have been published (Diefenbach et al., 2006; Franklin et al., 2011a; Keuthen et al., 2012). Second, this meta-analysis relied upon treatment-blind ratings to limit reporting bias. Although a notable strength, this resulted in the use of some outcome measures that had limited psychometric evaluation (e.g., video-taped hair loss ratings), and interchanged measures that evaluated symptom severity and impairment rather than focusing solely on the construct of symptom severity (Bloch et al., 2007). Finally, this meta-analysis separated treatment effects between CMI and SSRI medications. Although CMI can impact other neurotransmitters (e.g., norepinephrine reuptake inhibitor), it serves as a strong post synaptic serotonin reuptake inhibitor. As CMI and SSRIs both strongly affect serotonin receptors, there is some benefit to examining their collective efficacy, as well as their individual efficacy.

In an effort to address these limitations, this meta-analysis examined the efficacy of evidence-based treatments for individuals with TTM. Although antipsychotics and NAC have emerging empirical support, these treatments were considered too preliminary for inclusion due to the limited number of published RCTs. Thus, this meta-analysis examined the efficacy of BT and SRI treatment to reduce hair pulling severity among individuals with TTM. Additionally, clinically-relevant treatment moderators were examined that included: participant age; percentage of co-occurring anxiety and depressive disorders; outcome measure informant; average number of 1-h therapy sessions (for BT trials); study methodology; and intervention subtypes.

2. Method

2.1. Search strategy

PubMED (1965–March 2014), PsycInfo, and ProQuest Dissertations and Theses Online were searched using key search terms (i.e., “trichotillomania”, “habit reversal training”, “behavior therapy”, “behavioral intervention”, “competing response training”, “selective serotonin reuptake inhibitor”, or “serotonin reuptake inhibitor”). Identified titles and abstracts were reviewed independently by three raters for appropriateness. The references of eligible treatment trials, and review articles were also searched for published or unpublished research.

Identified abstracts/citations were evaluated for inclusion using the following criteria: (1) an RCT; (2) examined the efficacy of a BT or SRI in treating TTM relative to a non evidence-based comparison condition; (3) available in English; and (4) provided sufficient data to allow calculation of treatment effects. Trials were considered randomized when study authors explicitly represented them as such. Treatments were considered to be BT when they included awareness training and competing response training components. Treatments were considered to be an SRI when they included an antidepressant medication that inhibited the reuptake of serotonin (e.g., clomipramine, fluoxetine, sertraline). When treatment effect data was not sufficiently reported, study investigators were contacted to obtain values.

2.2. Meta-analytic procedures

2.2.1. Selection of outcome measures

Given that most studies employed multiple measures of TTM severity, a hierarchy of preferred TTM rating scales was established *a priori* to limit potential reporting bias. Although the Massachusetts General Hospital Hair pulling Scale (MGH-HPS; Keuthen et al., 1995; O'Sullivan et al., 1995) was commonly used, preference was placed on clinician-rated measures due to their standardized administration and objectivity. Three raters reviewed the published psychometric properties of standardized rating scales to determine the preferential order of clinician-rated, parent-report, and self-report ratings (Diefenbach et al., 2005a; McGuire et al., 2012). In order of preference, preferred clinician-rating scales included the National Institute of Mental Health-Trichotillomania Severity Scale (NIMH-TSS; Swedo et al., 1989), Psychiatric Institute Trichotillomania Scale (PITS; Winchel et al., 1992), and the Yale-Brown