



A meta-analysis of behavior therapy for Tourette Syndrome



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ABSTRACT

Individual randomized controlled trials (RCTs) of habit reversal training and a Comprehensive Behavioral Intervention for Tics (collectively referred to as behavior therapy, BT) have demonstrated efficacy in reducing tic severity for individuals with Tourette Syndrome and Chronic Tic Disorders (collectively referred to as TS), with no examination of treatment moderators. The present meta-analysis synthesized the treatment effect sizes (ES) of BT relative to comparison conditions, and examined moderators of treatment. A comprehensive literature search identified eight RCTs that met inclusion criteria, and produced a total sample of 438 participants. A random effects meta-analysis found a medium to large ES for BT relative to comparison conditions. Participant mean age, average number of therapy sessions, and the percentage of participants with co-occurring attention deficit hyperactivity disorder (ADHD) were found to moderate treatment effects. Participants receiving BT were more likely to exhibit a treatment response compared to control interventions, and identified a number needed to treat (NNT) of three. Sensitivity analyses failed to identify publication bias. Overall, BT trials yield medium to large effects for TS that are comparable to treatment effects identified by meta-analyses of antipsychotic medication RCTs. Larger treatment effects may be observed among BT trials with older participants, more therapeutic contact, and less co-occurring ADHD.

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1. Introduction

Chronic Tic Disorders and Tourette Syndrome (afterward collectively referred to as TS), are characterized by the presence of sudden motor movements and/or vocalizations (referred to as tics) that persist for more than a year. Tourette Syndrome commonly begins in childhood, increases in severity into early adolescence, and may persist into adulthood (Bloch and Leckman, 2009). Tic symptoms show little difference between youth and adults with TS, with common tics including eye blinking, head jerk movements, mouth movements, and simple vocalizations (McGuire et al., 2013). The estimated prevalence rate for TS in children ranges from three to eight per 1000 (Centers for Disease Control and Prevention, 2009). Individuals with TS frequently experience co-occurring obsessive compulsive disorder (OCD), non-OCD anxiety disorders, attention-deficit/hyperactivity disorder (ADHD), and/or disruptive

behaviors (Freeman et al., 2000). Tics and co-occurring conditions have been associated with functional impairment (Conelea et al., 2011, 2013), and a diminished quality of life (Jalenques et al., 2012; Storch et al., 2007).

Traditionally, TS has been managed with psychotropic medications such as antipsychotics and alpha-2 agonists (Scahill et al., 2006). A meta-analysis of five randomized controlled trials (RCTs) of antipsychotic medications identified a significant reduction in tic severity relative to placebo [standard mean difference (SMD) = 0.58], with no significant difference between medications (Weisman et al., 2012). Despite their efficacy, antipsychotics may be associated with side effects that may limit tolerability (Scahill et al., 2006). Alpha-2 agonists present another treatment option, with a meta-analysis of six RCTs identifying a more modest (SMD = 0.31), yet still significant benefit relative to placebo (Weisman et al., 2012). As a result, these medications are commonly recommended as a first-line treatment by professional organizations due to less severe side effects (Murphy et al., 2013).

Behavioral interventions have also demonstrated success in reducing tic severity (Verdellen et al., 2011). Among these interventions, only habit reversal training (HRT) has consistently

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demonstrated efficacy in RCTs. The core components of HRT are considered to be awareness training and competing response training (Miltenberger et al., 1998), with adjunctive therapeutic components including self-monitoring, relaxation training, contingency management, motivational procedures, and generalization training (Piacentini and Chang, 2006). Awareness training involves the detection of premonitory urges and/or early tic movements that precede a tic. Competing response training involves the identification of behaviors that are physically incompatible with a targeted tic, which are implemented upon early tic detection (e.g., premonitory urges, early tic movements). Habit reversal training serves as the principle therapeutic component in the Comprehensive Behavioral Intervention for Tics (CBIT) (Woods et al., 2008), which integrates HRT with functional assessment and function-based intervention procedures designed to mitigate influences of daily life that worsen tics. A related behavioral intervention called exposure and response prevention (ERP) involves exposure to sensations/urges that precede tics with response prevention of tics (Verdellen et al., 2004). These two treatments share similarities in terms of procedure (tic prevention) and mechanisms of change (habituation to urges), but are distinguished by the use of competing responses.

The efficacy of HRT and CBIT (afterward collectively referred to as behavior therapy, BT) has been supported across several RCTs with two noted exceptions (Azrin and Peterson, 1990; Deckersbach et al., 2006; O'Connor et al., 2001; Piacentini et al., 2002, 2010; Wilhelm et al., 2003; Wilhelm et al., 2012). One exception is a comparison trial of HRT to ERP. Participants in the ERP condition experienced greater reductions in tic severity that trended toward significance (Verdellen et al., 2004). Difference in duration of therapeutic contact hours may account for discrepancies as ERP participants received 24 therapeutic contact hours, whereas HRT participants received only 10. The other exception is a comparison trial of HRT to awareness training (a component of HRT), with results indicating only a minimal benefit of HRT above awareness training (Piacentini et al., 2002). While both of these trials compared BT to another active behavioral intervention, the remaining RCTs utilized waitlist or non-directive therapy as control conditions.

When making treatment recommendations, it is important to synthesize empirical evidence to guide clinical decisions (Murad and Montori, 2013). Meta-analyses provide a quantitative synthesis of treatment trials, and can examine moderators of treatment effects across studies. To date, only two meta-analyses have examined the efficacy of behavioral interventions for tics, albeit with noted limitations (Bate et al., 2011; Wile and Pringsheim, 2013). Bate et al., 2011 examined the efficacy of HRT across multiple habit disorders (e.g., TS, trichotillomania, nail biting, thumb sucking, stuttering, teeth grinding). While Bate et al. found HRT to have a large effect for TS (Cohen's $d = 0.78$), this examination had several limitations. For instance, Bate and colleagues excluded RCTs that used core BT components alongside adjunctive therapeutic components (O'Connor et al., 2001), and did not include a large trial of BT for TS (Wilhelm et al., 2012) or the comparison trial of HRT to awareness training (Piacentini et al., 2002). Furthermore, Bate and colleagues did not identify the measures used to extract treatment effects. As the psychometric properties of tic severity ratings scales differ from one another (McGuire et al., 2012), preference should be given to clinician-administered scales that have demonstrated reliability and validity.

Wile and Pringsheim (2013) examined the efficacy of BT for individuals with TS in two meta-analyses that each included two RCTs. On the clinician-rated Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989), Wile and Pringsheim (2013) found a difference in YGTSS Total Tic Scores between behavior therapy groups

and comparison groups of 3.66 and 10.52 for blinded and unblinded trials, respectively. Their examination of treatment response in two RCTs on the Clinical Global Impression of Improvement (CGI-Improvement; Guy and Bonato, 1970) identified an odds ratio in favor of BT. Despite its noteworthy contributions, this report had limitations that included a small sample size, utilization of a fixed effect model, and did not explore treatment moderators. Given the collective limitations of existent meta-analyses, further investigation is needed to comprehensively quantify treatment effects of BT, and explore moderators of treatment. A systematic approach to quantifying BT treatment effect is important because it facilitates comparison with existing pharmacotherapy meta-analyses for TS, and provides an informative comparison in the absence of a head-to-head RCT. Similarly, an examination of BT treatment moderators may inform clinical recommendations.

The present meta-analysis examined RCTs of BT to determine its efficacy in reducing tic severity and identify the odds ratio of treatment response. Additionally, this meta-analysis examined moderators of BT treatment effects that included: co-occurring OCD and ADHD; number of 1-h therapy sessions; participant age; methodological quality; and tic medication status.

2. Method

2.1. Search strategy

PubMed, PsycInfo, and ProQuest Dissertations and Theses Online were searched using key search terms (i.e., “behavior therapy” or “habit reversal” AND either “Tourette” or “chronic tic”). Identified abstracts were reviewed independently by two raters (JM, EB) for appropriateness. The references of eligible treatment trials, and review articles were also searched. Identified abstracts/citations were evaluated for the following inclusion criteria: (1) a RCT; (2) examined the efficacy of BT in treating TS; (3) available in English; and (4) provided sufficient data to allow calculation of treatment effects. Trials were considered randomized when study investigators explicitly represented them as such. Treatments were classified as BT when they included awareness training and competing response training. When treatment effect data was not sufficiently reported, study investigators were contacted to obtain values. If treatment effect data were unavailable for separate conditions and/or the authors did not respond to requests, the trial was excluded from analyses (Azrin et al., 1980).

2.2. Procedures

2.2.1. Outcome measures used to quantify treatment effects

Consistent with previous TS meta-analyses, a hierarchy of preferred tic rating scales for the primary outcome measure was established *a priori* to limit possible investigator reporting bias (Weisman et al., 2012). In order of preference, these tic rating scales included the YGTSS (Leckman et al., 1989), Tourette Syndrome Global Scale (Harcherik et al., 1984), Shapiro Tourette Syndrome Severity Scale (Shapiro and Shapiro, 1984), and Hopkins Motor/Vocal Tic Severity Scale (Walkup et al., 1992). In the absence of a standardized clinician-administered rating, direct observation of tics (e.g., tic frequency counts, ratings of tic severity) was used. Preference was given to in-clinic observations over home observations due to standardization of recording procedures.

2.2.2. Study coding

Trials were coded for the following characteristics: (1) sample size; (2) mean age; (3) percent of sample with ADHD and OCD; (4) percent of sample on tic medication; (5) average number of 1-

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