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Computerized response inhibition training for children with trichotillomania

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Abstract

Evidence suggests that trichotillomania is characterized by impairment in response inhibition, which is the ability to suppress pre-potent/dominant but inappropriate responses. This study sought to test the feasibility of computerized response inhibition training for children with trichotillomania. Twenty-two children were randomized to the 8-session response inhibition training (RIT; $n = 12$) or a waitlisted control (WLT; $n = 10$). Primary outcomes were assessed by an independent evaluator, using the Clinical Global Impression-Improvement (CGI-I), and the NIMH Trichotillomania Severity (NIMH-TSS) and Impairment scales (NIMH-TIS) at pre, post-training/waiting, and 1-month follow-up. Relative to the WLT group, the RIT group showed a higher response rate (55% vs. 11%) on the CGI-I and a lower level of impairment on the NIMH-TIS, at post-training. Overall symptom reductions rates on the NIMH-TSS were 34% (RIT) vs. 21% (WLT) at post-training. The RIT's therapeutic gains were maintained at 1-month follow-up, as indicated by the CGI-I responder status (= 66%), and a continuing reduction in symptom on the NIMH-TSS. This pattern of findings was also replicated by the 6 waitlisted children who received the same RIT intervention after post-waiting assessment. Results suggest that computerized RIT may be a potentially useful intervention for trichotillomania.

1. Introduction

Trichotillomania (TTM) is characterized by recurrent pulling of one's own hair with unsuccessful attempts to stop the behavior, resulting in hair loss, and significant physical and/or psychosocial impairment (Duke et al., 2010, Woods et al., 2006a). Despite its impact, TTM remains a poorly understood and underdiagnosed disorder for which effective and durable treatments are lacking; particularly in children (Duke et al., 2010).

Repetitive hair-pulling and failure to resist the urges suggests deficient response inhibition (RI) in TTM (Bohne et al., 2008, Chamberlain et al., 2006, Chamberlain et al., 2009). RI has received much attention as a cognitive deficit underlying TTM. RI enables one to suppress pre-potent or dominant responses that are no longer appropriate, which also constitutes a key component of executive control for flexible and goal-directed behavior (Aron et al., 2004, Verbruggen and Logan, 2008). Neuroimaging evidence indicates the right-lateralized inferior frontal cortex (rIFC) as a central locus of inhibition (Aron et al., 2004). A recent review has also suggested that rIFC and its associated networks function as a "brake" over response tendencies (Aron et al., 2014).

Research suggests a possible link between TTM and RI deficits. First, most behavioral studies in adult TTM have shown signs of RI deficiency on the Stroop (Bohne et al., 2005), go/no-go (Bohne et al., 2008), and stop/signal-tasks (Chamberlain et al., 2006). Further, a significant correlation between RI deficits (i.e., extended stop-signal reaction times) and TTM symptom severity was observed ($r = 0.56$, $p < 0.02$; Chamberlain et al., 2006). Second, TTM has been hypothesized to stem from deficits in cortical-striatal-thalamic-cortical circuits (Mataix-Cols and

van den Heuvel, 2006) and there are growing neuroimaging data supporting this view. Adults with TTM showed structural abnormalities in these regions, which are implicated in RI processes (van Velzen et al., 2014): abnormally increased grey matter densities in the left striatum, and several cortical regions (including frontal and supplementary motor) bilaterally (Chamberlain et al., 2008); excessive cortical thickness in neural regions relevant for RI, including the right inferior/middle frontal gyri (Odlaug et al., 2014); reduced basal ganglia volumes (O'Sullivan et al., 1997); reduced cerebellar volumes (Keuthen et al., 2007); reduced left inferior frontal gyrus volume (Grachev, 1997); and reduced white matter tract connectivity in prefrontal striatal circuitry involved in motor habit generation and suppression (Chamberlain et al., 2010). In contrast, there is a marked lack of behavioral and neuroimaging research on RI in pediatric TTM. Very few behavioral studies exist that have examined children with TTM vs. healthy controls on RI or related executive functions. Brennan et al. (2016) found that children with TTM performed better than healthy controls on the stop-signal task, although they had hypothesized escalated RI deficits in TTM. Another study reported impaired executive functioning in reversal learning, planning, and organization among children with TTM as compared with healthy controls (Flessner et al., 2016). Thus, there are very limited and mixed data regarding the deficits in RI and related cognitive functioning in pediatric TTM. Therefore, much research is needed to better understand RI processes in pediatric TTM, as the overall literature points to the importance of RI in TTM and its relevance for treatment of the disorder (Chamberlain et al., 2006, Chamberlain et al., 2009, van Velzen et al., 2014) with some even suggesting impaired RI as a candidate endophenotype of TTM (Odlaug et al., 2014).

Despite the documented benefits of behavior therapy (McGuire et al., 2014, Ninan et al., 2000, Woods et al., 2006a) and clomipramine (McGuire et al., 2014, Swedo et al., 1989), treatment literature for TTM is scarce and limited by numerous methodological issues (Woods et al., 2006a). This is particularly true in pediatric TTM, which is even more troubling considering that the estimated age of onset is 13 years and TTM characterized by an earlier age of onset tends to display poorer RI (Bohne et al., 2008). To enhance our field's understanding of TTM around its time of onset and facilitate treatment development, randomized controlled trial research focusing on a relevant treatment target is much needed (Harrison and Franklin, 2012). Despite the relevance of RI processes for TTM, no RI-focused cognitive intervention appears to exist for TTM.

We conducted a pilot clinical trial to examine the effect of a computerized cognitive training focused on improving RI processes for children with TTM. We predicted that systematic training of RI would result in the improvement in symptoms of TTM. Therefore, we hypothesized that, relative to the waitlist control, the RI training condition would show greater improvement in TTM symptoms and RI processes.

2. Method

2.1. Participants

We recruited children with TTM. A total of 45 children were phone-screened, and 27 underwent an onsite eligibility assessment. Informed consent was obtained from the parent or legal guardian of each participant prior to beginning the onsite eligibility assessment. They

were informed that this study aimed to test a computerized intervention designed to address the difficulty in inhibition of behaviors, which may help individuals with problematic repetitive behaviors. Inclusion criteria were (a) ages 9–17 years, and (b) primary diagnosis of TTM (DSM-IV criteria). Exclusion criteria included (a) active psychosis, (b) visual impairments (interfering with computer tasks), (c) parent-reported developmental disabilities, (d) low overall IQ (< 79), (e) unstable medication status (= change within 4 weeks prior to or during study), and (f) past/current substance use disorder. Twenty-two children met the study entry criteria and were randomized to the RI training (RIT; $n = 12$) or the waitlisted (WLT; $n = 10$) condition (See Fig. 1), utilizing computerized random numbers. Their average age was 13.18 (SD = 2.42). They were largely female (77.3%, $n = 17$) and Caucasian (86.4%, $n = 19$). Two children (1 in RIT, and 1 in WLT) discontinued the intervention (or waiting). Thus, data analysis included 20 children who completed the post-intervention/waiting assessment ($n = 11$ for RIT, $n = 9$ for WLT).
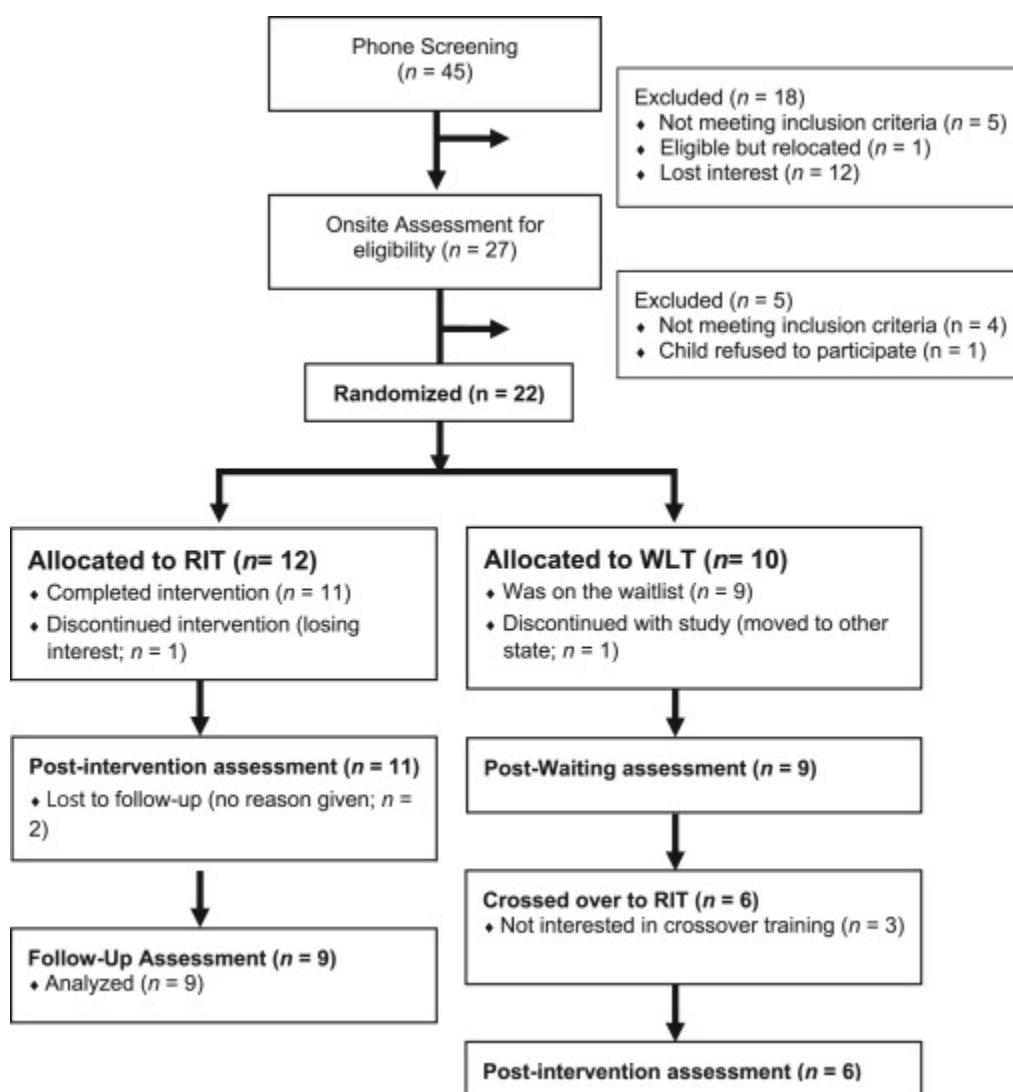

Fig. 1. Flow of study.

2.2. Measures

2.2.1. Treatment response status

The *Clinical Global Impression* Scale (CGI; Guy, 1976) is a clinician-rated scale for assessing the severity of the illness (CGI-S) and clinical improvement (CGI-I) from baseline on a 7-point scale. Scores of 1 (*very much improved*) or 2 (*much improved*) on the CGI-I were used to indicate a positive treatment response. The CGI was administered by a well-trained independent evaluator (IE) who was blind to the intervention conditions. The CGI has displayed good psychometric properties in child studies (De Los Reyes et al., 2011, Tolin et al., 2007), and has also been used as the main categorical outcome measure in existing psychosocial randomized controlled trials for pediatric TTM (Franklin et al., 2011, Morris et al., 2016).

2.2.2. Hair pulling symptoms

The National Institute of Mental Health *Trichotillomania* Questionnaire (NIMH-TQ; Swedo et al., 1989) is a clinician-administered scale for rating TTM symptoms, consisting of the Severity (NIMH-TSS) and Impairment (NIMH-TIS) scales. The NIMH-TSS assesses various aspects of TTM symptoms (i.e., time spent pulling, resistance to urges, overall distress, and interference) on a 0–5 scale. The NIMH-TIS offers a global assessment of functional impairment due to pulling on a scale from 0 (*no impairment*) to 10 (*severe*). The NIMH-TQ has demonstrated good psychometric properties in adults with TTM (Diefenbach et al., 2006, Stanley et al., 1999) and good test-retest and interrater reliability for children with TTM (Franklin et al., 2011). Further, the NIMH-TQ is sensitive to treatment-induced symptom change in adult TTM (Rothbaum, 1992, Woods et al., 2006b). It has also served as the primary outcome measure in existing psychosocial controlled trials for pediatric TTM (Franklin et al., 2011, Morris et al., 2016). In this study, a thoroughly trained and experienced master's level clinician served as a blinded independent evaluator (IE), and 25% of the recorded ratings were reviewed by an independent rater (interrater-rater agreement = 0.91 based on intraclass correlation coefficient).

The *Trichotillomania Scale for Children* (Tolin et al., 2008) is a widely-used 12-item hair pulling symptom scale with both child and parent versions (TSC-C and TSC-P), providing indices of Severity and Impairment, and their summed total score. The TSC has shown good psychometric properties (McGuire et al., 2012, Tolin et al., 2008).

2.2.3. Diagnostic measures

The *Trichotillomania Diagnostic Interview* (TDI; Rothbaum and Ninan, 1994) is a semi-structured interview to assess the DSM-IV criteria for Trichotillomania.

The *Anxiety Disorders Interview Schedule (ADIS) for DSM-IV - Child and Parent Versions* (Silverman and Albano, 2004) is a structured diagnostic interview that assesses major anxiety, mood, and externalizing disorders among children and adolescents aged 7–18. Youth and parents answer questions on the child and parent versions, respectively. The ADIS has

demonstrated excellent psychometric properties (Langer et al., 2010, Silverman et al., 2001, Wood et al., 2002).

2.2.4. Overall intellectual functioning

The *Wechsler Abbreviated Scale of Intelligence (WASI)* assesses intellectual functioning for individuals ages 6–89 years (Wechsler, 1999). The WASI produces a reliable estimate of an overall level of intellectual functioning.

2.2.5. RI assessment tasks

The *Stop Signal Task (SST)* was designed following the paradigm established and utilized for children (Carter et al., 2003, Lindqvist and Thorell, 2009). During the practice block, participants completed 15 go trials, requiring a prompt response to a red triangle on each trial. The main block presented 60 trials (2/3 were go-trials; 1/3 were stop trials displaying "Stop" following the go signal). The 60% duration of each child's mean RT (which was computed from the practice block for each child) was set as the stop-signal delay (i.e., the length of delay between the go stimulus and the stop signal), which was suggested as a theoretically meaningful interval for this paradigm to evaluate RI (Carter et al., 2003). The total number of commission errors (i.e., the erroneous response on the stop trial) served as the main index of RI deficits from this task.

The *Go/No-Go task* (Aycicegi et al., 2003, Lapierre et al., 1995, Lee et al., 2009) presented three, 40-trial blocks. Block 1 asked participants to promptly respond to a blue cross, to form a potent go-response tendency. In Block 2, participants were asked to respond promptly to the blue cross (2/3 of the trials), while inhibiting response to the blue star (1/3 of the trials). The target and distracter were reversed in Block 3 to increase the demand for inhibitory control. The total number of commission errors (i.e., erroneous response to the distracter) in Blocks 2 and 3 served as the RI index on this task.

2.2.6. Treatment acceptability

We administered self-reported items selected and adapted from the Treatment Acceptability Questionnaire (Hunsley, 1992) to explore the acceptability and tolerability of RIT: (a) acceptability, (b) ethicalness, and (c) acceptability of side effects (for both children and parents); and (d) pleasantness, and (e) distress (only for children). They were rated on a 7-point scale (e.g., Overall, how acceptable did you find the treatment to be? 1 = *very unacceptable* ~ 7 = *very acceptable*; How pleasant do you think this treatment was? 1 = *very unpleasant* ~ 7 = *very pleasant*).

2.3. Response inhibition training program (RIT)

Incorporating parameters of the go/no-go and stop-signal paradigms, RIT is a 30-level computer game, designed to provide systematic practice of RI focused on action withholding and action cancellation processes (Sebastian et al., 2013). Main task materials are simple geometric figures (e.g, blue/red squares and circles), comprising (a) go trial, (b) no-go trial, and

(c) stop trial. Participants practice withholding response to pre-potent stimulus (no-go trials) and cancelling ongoing response (stop trials), while selectively responding to appropriate targets. In each session, participants completed three 10-min game levels, each of which contained an average of 188 trials, with brief inter-level breaks. After completing each level, a result page was presented to summarize the participant's performance.

All children in RIT and 6 waitlisted children (who crossed over to RIT) completed all 8 sessions of training, spending 240 min in total with no variation across children. Training was conducted in a small therapy room in our Psychology clinic, using a laptop computer. After a research assistant (RA) set up the computer, the child completed the training session following instructions included within the training program. While staying at a comfortable distance from the participant, the RA remained in the room to assist the participant as needed and ensure the participants' adherence to the training program. However, all children completed the training procedures following the embedded instructions with very little assistance from the RA.

RIT is different from a mere repetition of existing go/no-go or SST in several important ways: (a) utilizing ascending levels, RIT becomes more difficult by systematically varying RI task parameters (i.e., increasing stop-signal delay latencies [the initial value was set at 200 ms and increased by an average of 12 ms at each level], and potentiating no-go trials by switching the shape/color of the stimuli); (b) RIT guides participants to make individually-tailored progress toward more difficult levels (i.e., each level is repeated until accuracy of 95% is reached); (c) RIT contains video-game features to increase participant's motivation (e.g., mastering levels and display of session record scores); and (d) RIT provides trial-by-trial performance feedback to help participants make conscious efforts to improve their ongoing RI performance.

2.4. Procedure

Participants who completed the baseline measures (including questionnaires, clinician-administered ratings, and RI assessment tasks) were randomized to RIT or WLT. The RIT group completed 8 twice-weekly sessions of training over a 4-week period, followed by a post-training assessment. The WLT group underwent post-waiting assessment after the 4-week waiting period. The primary outcome measures (i.e., CGI, NIMH-TSS, and NIMH-TIS) were administered by the blinded IE. The RIT group was assessed at 1-month follow-up again for the long-term outcome. Aside from the twice-weekly sessions, there were no between-session assignments or any further training during the follow-up period. For ethical considerations, following the post-waiting assessment, the WLT group was discontinued from the study and was offered the RIT intervention (i.e., cross-over training over 4 weeks). Completers were assessed to examine the outcomes of the cross-over training.

3. Results

3.1. Demographic and clinical characteristics at baseline

At pre-training, the RIT and WLT groups showed no significant differences on age, gender, race, overall intellectual functioning, the percentage of those with comorbid diagnoses (RIT = 27% [$n = 3$] vs. WLT = 44% [$n = 4$]), or the percentage of those receiving other treatments (RIT

= 18% [$n = 2$] vs. WLT = 33% [$n = 3$]. No group difference was found on the severity of TTM symptoms (the NIMH-TSS, TSC-P, and TSC-C) or the global severity of illness (the CGI-S). Overall, the two groups were equivalent (see Table 1).

Table 1. Baseline demographic and clinical characteristics.

	RIT (n = 11)		WLT (n = 9)			
	Mean	SD	Mean	SD	t (χ^2)	p
Age	12.91	2.39	13.11	2.52	0.18	0.86
Gender (% Male)	27% (n = 3)		22% (n = 2)		(χ^2 = 0.07)	0.80
Race White	100% (n = 11)		67% (n = 6)		(χ^2 = 4.31)	0.12
Asian	0% (n = 0)		22% (n = 2)			
African American	0% (n = 0)		11% (n = 1)			
Pulling Site						
Scalp	64% (n = 7)		78% (n = 7)			
Eyelashes	45% (n = 5)		44% (n = 4)			
Eyebrows	45% (n = 5)		11% (n = 1)			
Face	18% (n = 2)		11% (n = 1)			
Pubic	9% (n = 1)		11% (n = 1)			
Arms/Legs	18% (n = 2)		22% (n = 2)			
NIMH-TSS	10.45	2.51	11.11	2.57	0.58	0.57
NIMH-TIS	5.09	1.04	4.56	1.13	1.10	0.29
TSC-Parent Severity	1.31	0.55	1.29	0.33	0.10	0.93
TSC-Parent Impairment	0.87	0.56	1.04	0.58	0.67	0.51
TSC-Parent Total	2.18	1.00	2.33	0.76	0.37	0.71
TSC-Child Severity	1.18	0.48	1.22	0.37	0.21	0.84
TSC-Child Impairment	0.92	0.41	0.95	0.36	0.15	0.88
TSC-Child Total	1.96	0.76	2.06	0.78	0.29	0.77
CGI-Severity	4.36	0.50	4.33	0.50	0.13	0.90
WASI	112.18	10.40	111.33	12.51	0.17	0.87
Comorbidity Status						
Any comorbid diagnoses	27% (n = 3)		44% (n = 4)		(χ^2 = 0.64)	0.42
Major depressive disorder	9% (n = 1)		22% (n = 2)			
Generalized anxiety disorder	9% (n = 1)		11% (n = 1)			
Social anxiety disorder	9% (n = 1)		11% (n = 1)			
ADHD	9% (n = 1)		11% (n = 1)			
Current Treatment[a]	18% (n = 2)		33% (n = 3)		(χ^2 = 0.61)	0.44

	RIT (n = 11)		WLT (n = 9)			
	Mean	SD	Mean	SD	t (χ²)	p
Counseling/talk therapy	9% (n = 1)		11% (n = 1)			
Pharmacotherapy	18% (n = 2)		22% (n = 2)			
Stimulants	9% (n = 1)		11% (n = 1)			
Antidepressants	18% (n = 2)		22% (n = 2)			

Note. NIMH-TSS = the National Institute of Mental Health Trichotillomania Questionnaire Severity Scale; NIMH-TIS = the National Institute of Mental Health Trichotillomania Questionnaire Impairment Scale; TSC-Parent = the Trichotillomania Scale for Children - Parent Version; TSC-Child = the Trichotillomania Scale for Children - Child Version; CGI = the Clinical Global Impression Scale; WASI = the Wechsler Abbreviated Scale of Intelligence.

aCounseling was a general talk therapy for depression/anxiety symptoms for both children. There was no significant change in the treatment status in all participants throughout the study.

3.2. Response status on the CGI-I after training/waiting

Participants who were rated as 1 or 2 on the CGI-I at post-training were categorized as responders. The percentage of responders was 55% in the RIT group (*very much improved* [*n* = 4]), *much improved* [*n* = 2]), vs. 11% in the WLT group (*very much improved* [*n* = 1]). In a N-1 Chi-square test (Pearson, 1947), which is a sensitive and reliable test for a 2 × 2 contingency table with cells of low expected values (i.e., less than 5; Campbell, 2007), the response rate was significantly higher in the RIT, relative to the WLT group: N-1 χ^2= 3.90, *p* = 0.048.

3.3. Hair pulling on the NIMH-TSS and NIMH-TIS at post-training

In an ANCOVA, the RIT group showed a numerically lower total score on the NIMH-TSS than the WLT group at post-training after controlling for the baseline severity, but the difference was not statistically significant: RIT - Mean = 6.91 (SD = 4.37) vs. WLT - Mean = 8.78 (SD = 2.86), $F(1,17)$ = .84, *p* = 0.373, η^2 = .03 (small to medium effect size). Overall symptom reduction rates were 34% and 21% from the baseline level, for the RIT and WLT groups, respectively. The RIT group (mean = 2.50 [= *minimal impairment*], SD = 2.22) showed a significantly lower level of impairment on the NIMH-TIS than the WLT group (mean = 3.56 [= *minimal* to *mild impairment*], SD = 1.74) after controlling for the baseline level: $F(1,17)$ = 4.87, *p* = 0.041, η^2 = .14 (large effect size).[1]

3.4. Long-term outcomes at 1-month follow-up

Long-term outcomes were examined only for the RIT group as the WLT group did not take follow-up measures. On the CGI-I, the response status of the RIT group remained favorable at 1-month follow-up. Of the 6 responders at post-training, 5 completed the follow-up assessment and all of them maintained the responder status. Of the 5 non-responders at post-training, 4 completed the follow-up assessment and 2 of them became responders (very much improved

[*n* = 1], much improved [*n* = 1]). Thus, aside from one responder who was lost during the follow-up period, 7 out of 9 RIT follow-up completers (78%) were responders at follow-up (*very much improved* [*n* = 3], and *much improved* [*n* = 4]).

A similar pattern was observed on the NIMH –TSS. Among the 9 RIT study completers, compared to their baseline severity (mean = 10.89, SD = 2.57), symptom reduction rates were 33% at post-assessment (mean = 7.33, SD = 4.66) and 56% at follow-up (mean = 4.78, SD = 3.53). When considering all RIT participants, paired *t*-tests showed that their NIMH-TSS scores were significantly lower at post-training than at baseline, $t(10) = 3.36$, $p = 0.007$, d = 0.91 (large effect); and lower at follow-up than at post-training, $t(8) = 2.89$, $p = 0.020$, d = 0.57 (medium effect). These findings suggest continued symptom reduction during the follow-up period despite the discontinuation of the training.

3.5. Outcomes of the crossover RIT training

Of the 9 WLT participants, 6 received RIT after the post-waiting assessment. Prior to crossing over to RIT, all were deemed non-responders, but 4 of them (= 66%) became responders after the cross-over training (*very much improved* [*n* = 1], *much improved* [*n* = 3] on the CGI-I). For these 6 participants, the rate of symptom reduction from the baseline was 16.1% at post-waiting assessment. However, after the cross-over training, their pulling severity was further reduced by 52% from the baseline level on the NIMH TSS, which is comparable to the symptom reduction rate of the RIT group. The NIMH-TSS total score was significantly lower after cross-over RIT training (mean = 5.00, SD = 2.83), relative to the severity at post-waiting (mean = 8.67, SD = 3.20; $t(5) = 3.12$, $p = 0.026$, d = 1.21 [large effect]).

3.6. Self- and parent-reported symptom scores

Paired *t*-tests were conducted to examine changes in symptoms on the TSC-C and TSC-P (Table 2). In the RIT group, scores on the TSC-C Impairment, TSC-P Severity, TSC-P Impairment, and TSC-P Total were significantly lower at post-training than at baseline. These differences remained significant at 1-month follow-up. In the WLT group, a significant reduction at post-waiting was observed only on the TSC-C Impairment and TSC-C Total. Additionally, ANCOVAs were conducted to compare these scores at post-training/waiting while controlling for baseline levels. Relative to the WLT group, the RIT group showed a marginally significant trend of lower scores on the TSC-P Severity, $F(1, 17) = 3.70$, $p = 0.071$, $\eta^2 = .09$, and TSC-P Total, $F(1, 17) = 4.29$, $p = 0.055$, $\eta^2 = .08$. However, there were no group differences on the TSC-C Severity, $F(1,17) = 0.68$, $p = .42$, $\eta^2 = .03$, TSC-C Impairment, $F(1,17)=.003$, $p = 0.957$, $\eta^2 = .00$, TSC-C Total, $F(1,17) = .41$, $p = 0.53$, $\eta^2 = .01$, or TSC-P Impairment, $F(1, 16) = 1.40$, $p = 0.253$, $\eta^2 = .04$, at post-training.

Table 2. Scores on the TSC-C and TSC-P and paired *t*-tests on their change from baseline level.

	RIT			WLT		
	Pre	**Post**	**FU**	**Pre**	**Post**	**Crossover**
TSC-C Severity Mean	1.18	1.07	0.89	1.22	0.93	0.76

	RIT			WLT		
	Pre	**Post**	**FU**	**Pre**	**Post**	**Crossover**
(SD)	(0.37)	(0.52)	(0.49)	(0.37)	(0.45)	(0.52)
Pre vs. Post	$t(10) = 0.79$, $p = 0.449$			$t(8) = 1.84$, $p = 0.103$		
Pre vs. FU[a]	$t(8) = 1.84$, $p = 0.103$					
TSC-C Impairment Mean	0.92	0.66	0.59	0.95	0.66	0.85
(SD)	(0.41)	(0.46)	(0.49)	(0.36)	(0.36)	(0.56)
Pre vs. Post	$t(10) = 4.35^{**}$, $p = 0.002$			$t(8) = 2.47^{*}$, $p = 0.039$		
Pre vs. FU	$t(8) = 4.95^{**}$, $p = 0.001$					
TSC-C Total Mean	1.96	1.58	1.34	2.06	1.48	1.41
(SD)	(0.76)	(0.86)	(0.78)	(0.78)	(0.79)	(1.06)
Pre vs. Post	$t(10) = 2.25$, $p = 0.051$			$t(8) = 2.41^{*}$, $p = 0.043$		
Pre vs. FU	$t(8) = 3.57^{**}$, $p = 0.007$					
TSC-P Severity Mean	1.31	0.96	1.09	1.29	1.28	0.97
(SD)	(0.55)	(0.63)	(0.48)	(0.33)	(0.45)	(0.67)
Pre vs. Post	$t(10) = 2.38^{*}$, $p = 0.039$			$t(8) = 0.12$, $p = 0.911$		
Pre vs. FU	$t(8) = 2.89^{*}$, $p = 0.020$					
TSC-P Impairment Mean	0.87	0.50	0.54	1.04	0.81	0.60
(SD)	(0.56)	(0.43)	(0.41)	(0.58)	(0.57)	(0.16)
Pre vs. Post	$t(10) = 2.61^{*}$, $p = 0.028$			$t(8) = 2.28$, $p = 0.052$		
Pre vs. FU	$t(8) = 3.35^{*}$, $p = 0.010$					
TSC-P Total Mean	2.18	1.44	1.63	2.33	2.09	1.57
(SD)	(1.00)	(0.85)	(0.72)	(0.76)	(0.92)	(0.76)
Pre vs. Post	$t(10) = 3.47^{**}$, $p = 0.007$			$t(8) = 1.83$, $p = 0.104$		
Pre vs. FU	$t(8) = 3.67^{**}$, $p = 0.006$					

Note. Pre = pre-training assessment; Post = post-training/waiting assessment; FU = 1-month follow-up assessment; Crossover = post-crossover training assessment; TSC-Parent = the Trichotillomania Scale for Children - Parent Version; TSC-Child = the Trichotillomania Scale for Children - Child Version.

aPre vs. FU – These paired-*t*-tests compared the baseline vs. 1-month FU scores for the RIT group. This analysis was not conducted on the WLT group due to the absence of the follow-up assessment in this condition.

*p < 0.05.

**p < 0.01.

3.7. Changes in RI measures

3.7.1. SST

At baseline, there were no group differences on the indices of the SST: RT on Block 1, $t(18)$ = .21, p = 0.84, RT on Block 2, $t(18)$ = .1.15, p = 0.27, and overall commission errors, $t(18)$ = .49, p = 0.63. In an ANCOVA controlling for commission errors at pre-training and the current RT, the RIT group made significantly fewer commission errors than the WLT group at post-training, $F(1,16)$ = 7.39, p = 0.015, η^2 = .30 (large effect). Within the RIT group, commission errors were significantly lower at post-training than at baseline, $t(10)$ = 2.29, p = 0.045, but the number of commission errors at follow-up were not significantly lower compared to baseline, $t(8)$ =1.04, p = 0.328, or post-training level, $t(8)$ = 1.13, p = 0.290.

3.7.2. Go/No-Go task

There were no significant group differences on the number of commission errors, $t(16)$ = 1.28, p = 0.22, or overall RT, $t(16)$ = 1.41, p = 0.20 at baseline, or at post-training while controlling for baseline levels, $F(1,15)$ = .28, p = 0.60. Within the RIT group there were no significant reductions in commissions errors at post-training, $t(10)$ = 1.30, p = 0.22, or at 1-month follow-up, $t(8)$ = .86, p = 0.42 (see Table 3).

Table 3. Means and standard deviations of the RI measures.

	RIT			WLT		
	Pre	**Post**	**FU**	**Pre**	**Post**	**Crossover**
Stop-Signal Task						
Reaction Time Mean	577.68	647.75	638.82	661.04	671.78	608.19
(SD)	(156.11)	(157.34)	(166.47)	(180.41)	(242.71)	(175.91)
Commission Errors Mean	5.91	2.73	4.11	4.89	5.11	4.40
(SD)	(4.53)	(3.26)	(4.51)	(4.83)	(5.23)	(5.86)
Go/No-Go Task						
Reaction Time Mean	448.41	436.50	444.83	503.93	503.04	459.43
(SD)	(46.76)	(87.57)	(74.10)	(97.74)	(98.94)	(126.15)
Commission errors Mean	5.91	4.64	5.00	3.71	3.00	3.50
(SD)	(3.91)	(2.98)	(4.82)	(2.87)	(2.31)	(2.38)

Note. Pre = pre-training assessment; Post = post-training/waiting assessment; FU = 1-month follow-up assessment; Crossover = post-crossover training assessment.

3.8. Correlations between reductions in commissions errors and in pulling symptoms

We examined how pre-to post changes in RI indices were associated with pre-to post or pre-to follow-up changes in symptoms, utilizing their residual change scores (Table 4). The change

on the NIMH-TSS was not significantly correlated with changes in commission errors on both RI tasks. However, the pre-to post reduction on the NIMH-TIS showed moderate-sized correlations (= .30 ~ .36) with the reduction in commission errors on both RI tasks. On the TSC-C and TSC-P, pre-to post and pre-to follow-up reductions on their Impairment subscales showed moderate to large correlations (= .35 − .77) with reductions in commission errors on both RI tasks. These findings offer some preliminary evidence that the reductions in commission errors after the RI training can be positively associated with improvement on some indices of hair pulling symptoms, especially the level of impairment associated with hair pulling.

Table 4. Zero-order correlations (*p* values) between reductions in commission errors and reductions in symptom severity in the RIT group.

		Reduction in Commission Errors	
		Stop Signal Task	Go/No-Go Task
Pre-Post Sx Change	NIMH Total	0.19 (0.59)	0.25 (0.46)
	NIMH Global	0.30 (0.37)	0.36 (0.29)
	TSC-C Severity	−0.22 (0.52)	0.00 (0.99)
	TSC-C Impairment	0.49 (0.15)	0.77 (0.01)*
	TSC-P Severity	0.13 (0.70)	0.34 (0.30)
	TSC-P Impairment	0.35 (0.32)	0.42 (0.23)
Pre-FU Sx Change	NIMH Total	−0.02 (0.96)	0.1 (0.80)
	NIMH Global	0.19 (0.63)	−0.03 (0.93)
	TSC-C Severity	−0.19 (0.62)	−0.05 (0.89)
	TSC-C Impairment	0.53 (0.14)	0.51 (0.16)
	TSC-P Severity	−0.23(0.55)	0.07 (0.85)
	TSC-P Impairment	0.56 (0.12)	0.74 (0.02)*

Note. All reductions scores in this table are standardized residual change scores computed by regressing post-training scores onto their baseline scores.

*$p < 0.05$.

3.9. RIT acceptability and tolerability

Results showed that the RIT was overall well accepted and tolerated: (a) acceptability (Mean = 5.77, SD=1.42 for parents; Mean = 6.21, SD = 1.31 for children), (b) ethicalness (Mean = 6.62, SD = 0.96 for parents; Mean = 6.36, SD = 1.15 for children), and (c) acceptability of side effects (Mean = 6.73, SD = 0.90 for parents; Mean = 5.79, SD = 2.04 for children). Children also reported the RIT as overall pleasant (mean = 5.86, SD = 1.70) and non-distressing (mean = 5.79, SD = 1.12).

4. Discussion

Aiming to test the feasibility of RI training as a therapeutic intervention for youths with TTM, we observed encouraging preliminary data. At post-training, relative to WLT, RIT produced a significantly higher response rate (55% vs. 11%) and a significantly lower level of pulling-related impairment on the NIMH-TIS. Although the group difference on the NIMH-TSS did not reach statistical significance, the symptom reduction rate was also in the favor of RIT vs. WLT (34% vs. 21%). Relative to WLT, RIT also showed a marginally significant trend for lower parent-rated pulling severity (TSC-P). Further, acute training gains of RIT remained at 1-month follow-up. Aside from one RIT responder who was lost to follow-up, 7 out of 9 RIT completers (78%) were responders at follow-up. Notably, two out of 5 RIT non-responders at post-training achieved responder status at follow-up. Among these 9 RIT completers, the pulling severity (NIMH-TSS) continued to decrease during the follow-up period: symptom reductions rates were 33% at post-assessment and 56% at follow-up. These findings were replicated among 6 WLT children who completed the cross-over RIT. Although all of them were non-responders at post-waiting, 4 (= 66%) became responders after training, and their pulling severity decreased to 52% of the baseline level, similar to the therapeutic gains observed in the RIT group.

In the only randomized controlled trial of behavior therapy (BT) for children with TTM to date, Franklin and colleagues (2011) reported promising results of an 8-week BT protocol combined with an 8-week maintenance treatment (against a minimum attention control condition). At week 16, for the BT condition, the mean NIMH-TSS score was 2.5 (SD = 3.4) and 75% of the participants were responders on the CGI-I. Our 9 RIT study completers achieved overall comparable therapeutic gains at the end of the study: the mean NIMH-TSS = 4.8 (SD = 3.5) and response rate = 78% (7 out of 9 were responders) at follow-up. These findings are encouraging considering the brief, computerized, and portable format of the RIT. To date, moderate to large effect sizes have been reported from existing BT trials for adults and mixed samples (ages 16 and up) of TTM (Azrin et al., 1980, Diefenbach et al., 2006, Ninan et al., 2000, van Minnen et al., 2003, Woods et al., 2006a). Importantly, among the trials including follow-up assessments, several note a partial return of symptoms (Azrin et al., 1980, Franklin et al., 2011, Keuthen et al., 2012, Woods et al., 2006b) or eventual relapse (Diefenbach et al., 2006) over periods up to 22 months. Although this study only conducted a 1-month follow-up assessment, treatment response was maintained for the majority of participants, with some even displaying further improvement.

Consistent with our hypothesis, RIT showed significantly lower commission errors relative to WLT on the SST at post-training, which offers preliminary support for the RI-enhancing function of RIT. However, our findings on RI were overall mixed and should be interpreted with caution. Among RIT trainees, despite their reduction in TTM symptoms, the reduction in SST commission errors at post-training was attenuated at follow-up (i.e., not significantly different from the pre-training level any more), and a negligible reduction was observed in go/no-go commission errors. What are possible reasons for the discrepancy between the two RI tasks and the overall modest RI findings? Several issues need to be considered. First, although the RIT program includes both go/no-go and SST parameters (i.e., no-go trials and stop signals), the impact of its training might differ across the distinguishable RI components that are known to have both shared and *specific* neural subprocesses (Sebastian et al., 2013). Future

research needs to examine systematically whether a certain RI component (e.g., action cancelation assessed primarily by SST) is more amenable to change via RIT than others (e.g., action withholding assessed primarily by go/no-go).

Second, it is possible that behavioral RI may not reveal the full spectrum of changes in underlying RI processes, as compensatory responses at neural levels could emerge to obscure behavioral expressions of RI. Researchers suggest that the failure to find behavioral evidence of RI deficits can be due to compensatory brain activation during inhibition (van Velzen et al., 2014). Thus, modest changes in behavioral RI performance do not exclude the possibility of improved RI processes at neural levels. Future research should assess RI at neurocognitive levels including an fMRI assessment of RI-related neural circuit activity to obtain a fuller picture of changes in RI.

Third, it is possible that children with TTM may display only a limited facet of RI deficits, and cognitive deficits associated with TTM in adults may not emerge until later in the development (Brennan et al., 2016). Evidence also suggests that the main structure of executive functioning (including inhibition, shifting, and updating; see Miyake et al., 2000) remains undifferentiated in early childhood and become more specific and dissociable with age (Xu et al., 2013). Overall, the developmental neuroscience literature indicates that the inhibitory control function emerges rapidly during the first few years of life, followed by slow but continuing improvement through adolescence and early adulthood, with more localized, lateralized, and efficient brain activation in specific prefrontal cortex regions (e.g., left ventral PFC) relevant for inhibition (for a review, Best and Miller, 2010). Taken together, even well-established RI measures could suffer the problem of "task impurity" especially when applied to young individuals, due to the malleability of RI and its possible interaction with other related executive functions (e.g., working memory) over the course of development (Best and Miller, 2010, Xu et al., 2013), which might result in markedly variable (and thus less reliable) estimates of inhibition processes among children (Brennan et al., 2016). Thus, this line of research (a) critically needs more developmental sensitive measures of RI and (b) should assess RI while systematically considering its developmental trajectory using a much larger pediatric sample.

Fourth, the current potency of the RIT might have been insufficient to yield sufficiently large, enduring effects on behavioral RI performance. Future studies should attempt to establish (a) a criterion-level of RI change that is associated with clinically meaningful symptom change, and (b) the optimal dosage of RIT that can produce enduring, criterion-level change in RI.

Fifth, it is also possible that TTM symptom reductions have been promoted by other unassessed but TTM-relevant cognitive functions such as attention (e.g., Lee et al., 2012) improved by RIT. Overall, reduction in commissions errors on both the SST and go/no-go tasks were moderate- to largely correlated with reductions in hair pulling on the TSC scales, especially reductions in pulling-related impairment at follow-up, although the association was not pronounced with TTM severity. This is also aligned with the possibility that RIT may improve other RI-related cognitive processes, which may lead to overall improved functioning, beyond just those specific to pulling symptoms. Existing evidence also shows that pediatric TTM is characterized by impairments in other related executive functioning, including planning, organization, and reversal learning (Flessner et al., 2016). This study was underpowered to

conduct a formal mediational test to examine the mechanism of change in RIT, and was not able to assess other relevant cognitive processes due to the limited scope of the study. Thus, future research should conduct a formal mediation test with an adequate sample to elucidate the mechanism of change in RIT, including other measures of RI-related executive functioning and cognitive processes to establish the specificity of RI-focused intervention, and its possible transfer effects on untrained but adjacent functions.

Lastly, given the modest change in RI, we cannot exclude the possibility that the observed TTM reduction was merely reflecting RI-irrelevant non-specific factors such as expectation or attention from the staff. For the current pilot study, a waitlist was an appropriate control group in establishing the feasibility of the RIT, but future studies should include a more adequate comparison group to establish the specificity of RI-focused cognitive training while controlling for non-specific factors.

A few additional limitations and future directions of the study should be noted. First, we cannot exclude the influence of other unintended factors on the RIT outcomes at follow-up (e.g., spontaneous recovery or repeated assessment), as the WLT control group crossed over to RIT without a comparable follow-up assessment. Second, despite the promising results, this is a pilot feasibility study with a small clinical sample comprising of predominantly Caucasian females. Consequently, the current study was not adequately powered to detect modest intervention effects of RIT on some important outcome variables such as TTM symptom severity as assessed by the NIMH-TSS. Take together, replications with larger, more representative clinical samples are critically needed to more adequately evaluate the size of RIT effects and their statistical and clinical significance, as well as its underlying mechanism of action.

In sum, the current pilot study demonstrated the feasibility of the RIT as a potentially effective intervention for children with TTM. Considering the developmental trajectory of RI and its malleability during childhood/adolescence, the effort to develop an intervention specifically focused on this cognitive deficit for young individuals with TTM seems theoretically and clinically important. If successful, this line of work can also lead to the development of a cost-effective, time-efficient, and portable form of clinical intervention for TTM in particular, and perhaps for other numerous conditions sharing RI deficits as an underlying cognitive deficit. A successfully developed RIT may also be easily disseminated using various technology platforms and utilized as a stand-alone treatment or as an adjunctive intervention for existing treatments. Future research for RIT seems warranted to demonstrate its efficacy in a larger clinical scale and examine its specific mechanism of action.

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We also conducted intent-to-treat analyses on the primary outcome measures at post-training assessment, including all randomized children (N = 22) based on the well-established multiple imputation procedure (Graham, 2009). Twenty data sets were imputed using the MICE

package of R, and pooled estimates were computed. Overall pattern of findings remained identical: for the NIMH-TSS (F[1, 3540.74] = 1.34, p = 0.247), the NIMH-TIS (F[1, 1432.96] = 4.85, p = 0.028), and CGI-I response rate (F[1, 2739.59] = 3.98, p = 0.046; the significance test for combined Chi-square values uses an F distribution, see Robitzsch et al., 2017).