Cognitive behavioral management of Tourette’s syndrome and chronic tic disorder in medicated and unmedicated samples

Kieron P. O’Connor*1, Anick Laverdure, Annie Taillon, Emmanuel Stip, François Borgeat, Marc Lavoie*

Fernand-Seguin Research Centre, Louis-H. Lafontaine Hospital 7331 Hochelaga St. Montreal (Quebec) H1N 3V2 Canada

Objective: Cognitive behavior therapy (CBT) and medication can be administered in combination in treating tic disorders but there are no studies evaluating the effectiveness of CBT with and without medication. The current study compares the efficacy of CBT in combination with medication and without medication.

Method: CBT was administered in a consecutively referred sample of 76 people diagnosed either with Gilles de la Tourette Syndrome or chronic tic disorder. The sample was divided into a medicated and a non-medicated group. Twenty-three were stabilized on medication and 53 were not receiving medication. Measures administered pre- and post-CBT in both groups included: main outcome measure of Tourette Syndrome Global Scale and measures of mood.

Results: Repeated measures analysis of variance on the initial sample revealed no difference between medicated and non-medicated groups in outcome. A further analysis comparing the 23 receiving medication with 23 not receiving medication matched on baseline clinical variables also yielded no significant group differences, either in treatment outcome on main tic outcome measures or on other clinically relevant questionnaires.

Discussion: CBT for tic disorders is an effective treatment administered either in combination with medication or alone.

Introduction

Gilles de la Tourette syndrome (TS) and chronic tic disorder (TD) are disabling neuropsychiatric conditions characterized by multiple motor and/or phonic tics (APA, 2000). Although severity of the disorder is assessed according to severity of tics, other comorbidities and behavioral problems may complicate the clinical management (Leckman et al., 1998). Distinct comorbidities may be present at distinct periods of development and although tics are at their peak in childhood, they continue into adulthood and may even show late life onset (Bloch et al., 2006). Aetiology is multi-faceted showing at the same time genetic, biological, and environmental influences. Both medication and cognitive behavior therapy (CBT) have shown effective treatment. Since the first discovery of Seignot (1961), the medication of choice for TS is generally small doses of neuroleptic medication such as Haldol or Risperidone (Dion, Annable, Sandor, & Chouinard, 2002) based on a neurobiological model of dopamine dysregulation (Ernst et al., 1999; Singer, Hahn, & Moran, 1991; Singer et al., 2002). However, no single medication suits all, and a wide range of medications are frequently prescribed for tic management including antidepressants and tranquilizers. Such medications may also be prescribed to manage common comorbidities involving behavioral disturbance or mood regulation (Scahill et al., 2006).

CBT is based essentially on behavioral principles which view tics as maintained either by positive reinforcement (e.g., receiving attention), or negative reinforcement (e.g., through release of tension and pre-monitory urge) or by auto-reinforcement (habit formation). CBT focuses on functional analysis and management of environmental contingencies (Verdellen, Hoogduin, & Keijers, 2007; Verdellen, Keijers, Cath, & Hoogduin, 2004; Woods et al., 2008). The oldest CBT approach is habit reversal (Azrin & Nunn, 1973) based originally on a learning model (Woods & Miltenberger, 2001). This model currently addresses management of contingencies and implementation of an antagonist or competing response. Other behavioral approaches have proposed that tics be considered as responses to pre-monitory urges which need to be tolerated according to an exposure and response prevention model (Verdellen et al., 2007). Recent work has also targeted the role of cognitive as well as behavioral factors in provoking and maintaining tics (O’Connor, 2002). Small scale randomized clinical trials have established the efficacy of behavioral approaches,
either compared with waitlist or non-specific treatment (Deckersbach, Rauch, Buhlmann, & Wilhelm, 2006; O’Connor et al., 2001; Woods et al., 2008). These approaches have demonstrated clinically significant improvement following behavioral management of tics and at the same time have suggested that the urge to tic may also be modifiable. In resume, both CBT and medication are effective treatments for TS and TD.

Medication and CBT are frequently administered in conjunction but as of present, there is no literature examining any synergistic benefit of combining treatments. The present study evaluates whether CBT is equally effective when combined with existing medication or administered in the absence of medication.

Method

Aim

The aim of the present study was to compare the effectiveness of CBT in the presence and absence of medication. Outcome in two groups of TS and TD, both receiving identical CBT, was compared. One group was medication free and was not receiving any medication for tics or comorbid disorders at the time of therapy or for at least eight months prior to therapy, while the other group was medicated and stabilized for a minimum of three months prior to entry in the treatment program. Since CBT and pharmacotherapy are based on distinct models of action, the hypothesis was that CBT would be as effective in reducing tics in the presence of medication and without medication.

Participants

Seventy six consecutive referrals were chosen from participants in a CBT program for tic disorders at Centre de Recherche Fernand-Seguin, Montréal (2003–2007). The participants were enrolled in one of two clinical trials involving natural waitlist control and which are reported elsewhere (O’Connor, Lavoie, Stip, Borgeat, & Lavender, 2008; O’Connor, Lavoie, Goulet, & Koszegi, in preparation). All participants were adults (18–65) who fulfilled diagnostic criteria for TS or TD according to the DSM-IV-TR (American Psychiatric Association, 2000: [307,23]), including the presence of multiple motor tics and at least one or more vocal tic for the TS group, while only one motor or vocal tic needed to be present for the TD group. Simple motor tics are sudden, brief, meaningless movements. Complex motor tics are more purposeful stereotyped movements of longer duration, such as facial gestures and grooming-like movements. Simple phonic tics are fast, meaningless sounds or noises, while complex phonic tics may include syllables, words or phrases, as well as odd patterns of speech. Diagnosis was based on a consensus between a certified psychiatrist (E.S., F.B.) and a team clinical psychologist supervised by K.O. The Clinical Interview for DSM-IV (SCID-IV: First, Spitzer, Gibbon, Williams, & Benjamin, 1996) or the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV: Brown, Di Nardo, & Barlow, 1994) were also administered. Exclusion criteria for all participants included the presence of a primary diagnosis, other than TS or TD, on axis I (comorbid mood disorders [anxiety and depression] were included if in the mild range; score below 19 on Beck Depression Inventory [BDI-II] and below 16 on the Beck Anxiety Inventory [BAI]) or the presence any other severe problem as rated on axis II, III, IV or V of the DSM-IV-TR. Participants currently receiving any other form of non-pharmacological treatment for their tic symptoms and receiving a course of medication other than for tic disorders were also excluded. Symptom severity and treatment outcome was also assessed using the “Tourette Syndrome Global Scale” (TSGS: Harcherik, Leckman, Detlor, & Cohen, 1984). The TSGS tic subscales rate the nature of the tic (i.e. motor or phonic), and the tic complexity. Behavioral subscales assess functional impairment, including learning, motor restlessness and occupational problems. Both scales were included in the global score. The inter-rater reliability of the TSGS global score was found to be very good (k = 0.77, p < 0.001). The motor and phonic tic subscale showed convergent validity with the corresponding Yale global tic severity scale, with correlations ranging from r = 0.86 to r = 0.91 (Leckman et al., 1989). The SCID-IV, ADIS-IV and TSGS were administered by doctoral level psychologists trained in psychiatric evaluation who evaluate a range of disorders for diverse clinical studies. Prior to pre-treatment evaluation, they were blind to any prior diagnostic status and did not receive screening information, and post-treatment they were blind to treatment status (post-natural waitlist or post-treatment assessment). The maximum total of the TSGS is 100, mild scores 0–24, moderate 25–39, severe 40–59, and extreme 60–100 (Harcherik et al., 1984). Participants in the medicated group obtained TSGS scores distributed across mild (48%), moderate (35%), severe (9%) and extreme (8%) symptom intensity, whereas participants in the non-medicated group obtained TSGS scores distributed across mild (68%), moderate (28%) and severe (4%) symptom intensity. The sample included both mild and severe cases but the majority of participants were functioning adults with good adjustment to their disorder. So, although the median TSGS scores fell in the moderate range, the median score on the TSGS tic subscale was in the range representative of tic disorder samples (Harcherik et al., 1984).

Twenty three participants were stabilized on medication for their tics prior to CBT and throughout the CBT trial and 53 were not receiving medication and had not received medication at least eight months prior to entry into the study, either because they were drug naïve (n = 28) or because medication had ceased (n = 25). The list of medications is given in Table 1. The medications included typical and atypical neuroleptics, antidepressants, anti-anxiety, muscle relaxants and stimulants. Twelve participants were receiving one medication, eight participants were receiving two medications and three participants were receiving three medications. All medications were prescribed specifically for TS or TD or associated problems. Those on medication had been stabilized for a minimum of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>List of medications.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressant</td>
<td>Atypical neuroleptic</td>
</tr>
<tr>
<td>Paroxetine (n = 3)</td>
<td>Risperidone (n = 5)</td>
</tr>
<tr>
<td>Sertraline (n = 2)</td>
<td>Pinonide (n = 1)</td>
</tr>
<tr>
<td>Valproate (n = 2)</td>
<td>Quetiapine (n = 1)</td>
</tr>
<tr>
<td>Fluoxetine (n = 2)</td>
<td>Venlafaxine (n = 2)</td>
</tr>
</tbody>
</table>

Unmedicated sample: 28 participants of the total unmedicated sample and 20 participants of the matched sample were medication naïve while the others had taken medication for tic disorders at some point in their life but were not taking any at the time of the CBT trial.
In the current study, assessments were conducted at pre- and post-treatment for all outcome measures. All participants completed pre- and post-treatment questionnaires assessing depression (Beck Depression Inventory [BDI]; Beck, Rush, Shaw, & Every, 1979); anxiety (Beck Anxiety Inventory [BAI]; Beck, Epstein, Brown, & Steer, 1988); obsessive-compulsive symptoms (Penn State Obsessive Compulsive Scale [P SoCS]; Foa & Kozak, 1986); and adult overactivity (Style of planning) [STOP] questionnaire (O’Connor, 2005a). The STOP questionnaire has two subscales, overactivation and overpreparation, and discriminates satisfactorily between tic disorders and other psychiatric populations. A more negative score indexes greater pathology. These questionnaires measured states clinically relevant to TS and TD. Clinical and questionnaire data are given in Table 4. The PI was included as additional screening for comorbid obsessive compulsive disorders.

**Cognitive behavioral treatment**

The current CBT was individualized, manual-based (O’Connor, 2005b), and was carried out by therapists who were licensed psychologists with 10 years experience of CBT with tic disorder and OCD. The program was progressive and passed through seven major steps, lasting a total of four months: psychoeducation, awareness training, constructing a high/low risk situational/activity profile, relaxation and muscle discrimination exercises, modifying background style of planning action, development of alternative competing responses using cognitive and behavioral strategies, and preventing relapse. The present program, whilst building on components of a habit reversal package, differs from conventional habit reversal in two ways. Firstly, the program includes cognitive and behavioral restructuring as part of the habit reversal. So for example, while an antagonist response in habit reversal might be limited to a muscle contraction (see Carr, 1995), in the current approach the key habit reversal strategy of implementing a competing behavioral response to the tic/habit was developed alongside a more general cognitive and behavioral restructuring of the person’s approach to the high-risk tic situation, which addressed anticipations, meta-cognitions and appraisals concerning the appearance of the tics (e.g., reversing a shoulder movement contraction as part of an overall more relaxed posture and attitude when talking). The cognitive aspect of restructuring action and planning action aimed to introduce flexibility into judgments and anticipations about intended action, both in high-risk and other situations.

Retraining in planning action is an additional cognitive remediation strategy based on neurophysiological findings, which reported evidence of difficulties in TS and TD groups in the preparation and planning stage of action (but not in execution) (O’Connor, Lavoie, Robert, Stip, & Borgeat, 2005; O’Connor et al., 2008; Thibault, O’Connor, Stip, & Lavoie, 2009). As part of the behavioral strategy of retraining sensori-motor activation, overactive style of action (see O’Connor, 2002) was specifically addressed, including: the efficacy of concentrating on one task at a time and screening out distractions;
countering thoughts likely to lead to overactive performance; developing realistic feedback on performance ability; avoiding strategies that create tension and frustration (e.g., trying always to be further advanced and "ahead of oneself" in performance; structuring a timetable efficiently). A previous study showed that post-treatment success in modifying the style of action component was associated with successful outcome (O'Connor et al., 2001). This style of action was monitored by the STOP questionnaire. The entire treatment package was administered for a standard period of 12 weekly sessions with a further 1-month home practice prior to full post-treatment evaluation (see O'Connor et al., 2001).

Efficacy of CBT program versus waitlist control

This CBT program has been shown more effective compared to a randomized waitlist control group (O'Connor et al., 2001, 2008) and in the current trial, tic status did not change significantly over comparable natural waitlist periods with a multiple baseline control (p < 0.20) (O'Connor et al., in preparation).

Results

Analysis

In order to test the hypothesis, outcome for both tic symptom measures and other measures of mood and style of planning was compared pre- and post-CBT by repeated measures mixed model (fixed and random factors) analyses of variance with treatment (pre–post) and group (medication vs non-medication) as main factors. Significance levels were set at p < 0.05. Effect sizes were calculated as partial eta squares.

Baseline

An initial comparison of those receiving and not receiving medication in the total sample (n = 76) showed no significant difference between the two groups at baseline in gender, age, referral, civil status, children, occupation, education, other family members with tics, and co-morbidity. Obsessionality as measured by the Padua was low in both groups (medicated: 35.9 [218]; unmedicated: 31.3 [208]). There was however a difference in clinical severity at baseline as measured by the TSGS total score with the medication group showing higher severity, t(74) = 2.67; p < 0.05 (see Table 4).

Outcome

TSGS total scores decreased significantly in both groups (medicated group: F[1,22] = 26.44; p < 0.05; effect size = 0.55; unmedicated group: F[1,52] = 49.95; p < 0.05; effect size = 0.49). The overall percentage improvement on total TSGS scores pre–post CBT was 49% for medicated and 54% for unmedicated groups.

Both the TSGS tic subscale and behavior subscale showed a significant decrease in both groups (tic subscale, medicated group: F[1,22] = 25.04; p < 0.05; effect size = 0.53; tic subscale, unmedicated group: F[1,52] = 56.10; p < 0.05; effect size = 0.52; behavior subscale, medicated group: F[1,22] = 15.58; p < 0.05; effect size = 0.42; behavior subscale, unmedicated group: F[1,52] = 19.76; p < 0.05; effect size = 0.28) and no TSGS subscale showed any significant interaction effect. There was a group by treatment outcome interaction effect for total TSGS score (F[1,74] = 5.36; p < 0.05; effect size = 0.51). Entering baseline total TSGS score as covariate eliminated group by treatment interaction effects, leaving only a main treatment effect (F[1,73] = 15.73; p < 0.00; effect size = 0.18).

There was a significant improvement (decrease) in BAI scores in the unmedicated group (F[1,52] = 15.28; p < 0.05; effect size = 0.23) but not in the medicated group (F[1,22] = 1.56; p = 0.26, ns; effect size = 0.07). There was a significant improvement in BDI scores in both groups (medicated group: F[1,22] = 7.44; p < 0.05; effect size = 0.25; unmedicated group: F[1,52] = 7.49; p < 0.05; effect size = 0.13). Both depression and anxiety scores were numerically higher in the medicated group pre–treatment, but no scores were in the clinically significant range. There was a significant improvement in total STOP scores in the medicated group (F[1,22] = 6.41; p < 0.05; effect size = 0.23) but not in the unmedicated group (F[1,52] = 0.53; p = 0.47, ns; effect size = 0.01) (see Table 4).

Further analysis of matched subsamples

To control for differences in baseline severity between the two samples, the medication group was matched to a non-medication subgroup on the basis of TSGS total (tic and behavior) symptom severity. This reduced the N to 23 participants in each of the medication group and non-medication subgroup (see Table 3). Twenty of the 23 patients in the matched non-medication subgroup were drug naive, reporting never receiving pharmacotherapy, and only two of the remaining had received medication (in both cases clonazepam) during the year prior to entering the CBT trial. Clinical data for the matched groups are shown in Table 5.

Repeated measures mixed model analysis of variance of the matched samples yielded significant main treatment effects for TSGS scales (total: F[1,44] = 54.10; p < 0.05; effect size = 0.56; Tic: F[1,44] = 56.93; p < 0.05; effect size = 0.56; Behavior: F[1,44] = 31.89; p < 0.05; effect size = 0.42); BAI (F[1,44] = 10.86; p < 0.05; effect size = 0.20); BDI (F[1,44] = 13.84; p < 0.05; effect size = 0.24); STOP total (F[1,44] = 5.26; p < 0.05; effect size = 0.11) and overactivation (F[1,44] = 12.57; p < 0.05; effect size = 0.22) and overpreparation (F[1,44] = 4.78; p < 0.05; effect size = 0.10) subscales. No interaction effects approached significance for any scales or subscales.

Results for each group separately were: Medicated group: TSGS total (F[1,22] = 26.44; p < 0.05; effect size = 0.55); tic subscale (F[1,22] = 25.04; p < 0.05; effect size = 0.53); Behavior (F[1,22] = 19.43; p < 0.05; effect size = 0.47); BAI (F[1,22] = 15.56; p < 0.21; ns); BDI (F[1,22] = 7.44; p < 0.05; effect size = 0.25); STOP total (F[1,22] = 13.54; p < 0.05; effect size = 0.38); overactivation subscale (F[1,22] = 11.56; p < 0.05; effect size = 0.34) and overpreparation subscale (F[1,22] = 10.85; p < 0.05; effect size = 0.33).

Unmedicated group: TSGS total (F[1,22] = 28.76; p < 0.05; effect size = 0.57); tic subscale (F[1,22] = 32.27; p < 0.05; effect size = 0.60), and behavior subscale (F[1,22] = 12.92; p < 0.05; effect size = 0.37); BAI (F[1,22] = 13.09; p < 0.05; effect size = 0.37); BDI (F[1,22] = 6.49;

### Table 5
Clinical variables – matched groups.

<table>
<thead>
<tr>
<th></th>
<th>Medicated (n = 23)</th>
<th>Unmedicated (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre Mean (SD)</td>
<td>Post Mean (SD)</td>
</tr>
<tr>
<td>TSGS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tics</td>
<td>13.57 (9.78)</td>
<td>9.74 (5.05)</td>
</tr>
<tr>
<td>Behavior</td>
<td>14.17 (10.37)</td>
<td>14.35 (8.50)</td>
</tr>
<tr>
<td>Total</td>
<td>27.75 (17.18)</td>
<td>24.19 (11.60)</td>
</tr>
<tr>
<td>BAI</td>
<td>11.20 (11.53)</td>
<td>10.29 (9.60)</td>
</tr>
<tr>
<td>BDI</td>
<td>10.12 (8.37)</td>
<td>8.13 (9.17)</td>
</tr>
<tr>
<td>STOP – Total</td>
<td>-0.62 (9.10)</td>
<td>-0.10 (7.43)</td>
</tr>
<tr>
<td>STOP – Overactivation</td>
<td>4.50 (6.00)</td>
<td>5.66 (7.36)</td>
</tr>
<tr>
<td>STOP – Overpreparation</td>
<td>-0.09 (8.76)</td>
<td>3.57 (7.08)</td>
</tr>
<tr>
<td>STOP – Total score</td>
<td>1.76 (28.75)</td>
<td>15.68 (24.24)</td>
</tr>
</tbody>
</table>

TSGS: Tourette Syndrome Global Scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; STOP: Style of Planning Questionnaire.

1. The BAI, BDI and STOP scores were transformed due to kurtosis.
p < 0.05; effect size = 0.23); STOP total (t[1,22] = 0.00; p = 0.97; ns), overactivation subscale (t[1,22] = 2.65; p = 0.12; ns) and over-preparation subscale (t[1,22] = 0.05; p = 0.82; ns).

The percentage improvement in principal outcome measures after CBT did not differ significantly in the non-medicated and the medicated group. Residual gain scores pre- and post-treatment were also not significantly different between the medicated group and non-medicated subgroup for total TSGS score (t[44] = −0.06; p = 0.96, ns), tic subscale (t[44] = 0.268; p = 0.80, ns) and TSGS behavior subscale (t[44] = 0.94; p = 0.35; ns).

**Discussion**

The current study, to our knowledge, is the first to compare the effect of CBT with and without medication in a sample of TS and TD adults. The key finding was that principal outcome measures (TSGS subscales) for both TS and TD stabilized on medication at time of receiving CBT and those not taking medication at the time of receiving CBT, showed significant and equivalent improvement. This finding held in differing degrees in both the original sample (n = 76) and the matched sample (n = 46) for all subscales of TSGS plus other clinically relevant measures of depression and anxiety. Essentially, the hypothesis that CBT is as effective in the presence or absence of medication was supported. The implication is that CBT can be effectively administered whether or not the client is stabilized on medication, and whether or not the tics are severe, moderate or mild.

Limitations of the study are that although all medications were stabilized, the type of medication was not controlled, hence people were on a range of medications. The effect of medication itself on tic frequency was not assessed. Clearly the higher initial baseline level of symptom severity in the medication group could reflect the likelihood of those with more severe symptoms receiving medication. Since the medication sample was already stabilized on medication prior to CBT, it is possible that the medication had already reduced tics in this group to a manageable level, so permitting CBT to effect further reduction. Furthermore the level of severity and co-morbidity was not extreme due to exclusion criteria. The study was not designed to evaluate the effects of medication on TS/TD nor to compare CBT to medication, but rather just to permit conclusions on the effectiveness of CBT administered concurrently to participants with and without medication. Further studies could directly compare the effect of medication and CBT in head to head comparisons. Although change in the style of action measures was in the positive direction post-treatment in both groups, these changes failed to reach significance in the non-medicated group. This finding might indicate the value in future of examining the effect of medication on distinct process variables and components within the CBT program, not reflected in overall outcome measures.

Another future area of study is the effect of CBT on cerebral processes. As noted in the introduction, it is generally presumed that CBT and pharmacotherapy operate through distinct mechanisms and this fact might explain their complementarity. Several studies show that following CBT, cerebral activity associated with psychiatric states may become less pathological (see Cozolino, 2002; Schwartz & Begley, 2002) such as in OCD (Brody et al., 1998; Saxena et al., 2009) and in phobia (Paquette et al., 2003).

Our own results have shown that CBT significantly affects response processing, particularly fine motor dexterity revealing that CBT selectively improved motor performance compared to a waitlist control, and this improvement was correlated to clinical outcome measures (O’Connor et al., 2008). Other results revealed that frontal event-related brain activity, associated with automated motor responses, are improved after successful CBT in TS, revealing that CBT might have some impact on cerebral function that parallel symptom improvement (Lavoie et al., 2008). Finally, combined pharmacotherapy and CBT treatments of TS children are very common (see Sukhodolsky et al., 2003), but there is surprisingly little consistent information on the combined use of CBT in children (Placenti & Chang, 2001; Poncin, Sukhodolsky, McGuire, & Scähill, 2007).

**Acknowledgments**

This work was supported by a Canadian Institutes of Health Research (CIHR) operating grant (MOP57936), a Fonds pour la Recherche en Santé du Québec (FRSQ), clinical research grant (5271) and the laboratory infrastructure grant from the Fernand-Seguin Research Center. We wish to express our gratitude to Marie-Claude Pélissier, Frederick Aardema, Ariane Fontaine and Valérie Poulin for research coordination and clinical screening, as well as to Emilie Pressuto and Monique Lahoud who acted as independent raters. Finally, we thank all participants for their participation in this study.

**References**


