Evaluation of Inference-Based Cognitive-Behavioral Therapy for Obsessive-Compulsive Disorder: A Multicenter Randomized Controlled Trial with Three Treatment Modalities

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Keywords
Obsessive-compulsive disorder · Cognitive-behavioral therapy · Inference-based approach · Mindfulness · Randomized controlled trial

Abstract
Introduction: Inference-based cognitive-behavioral therapy (I-CBT) is a specialized psychological treatment for obsessive-compulsive disorder (OCD) without deliberate and prolonged exposure and response prevention (ERP) that focuses on strengthening reality-based reasoning and correcting the dysfunctional reasoning giving rise to erroneous obsessive doubts and ideas. Objective: The present study aimed to evaluate the effectiveness of I-CBT through a comparison with appraisal-based cognitive behavioral therapy (A-CBT) and an adapted mindfulness-based stress reduction (MBSR) intervention. Methods: This was a two-site, parallel-arm randomized controlled trial (RCT) comparing I-CBT with A-CBT. The MBSR intervention acted as a non-specific active control condition. Following formal evaluation, 111 participants diagnosed with OCD were randomly assigned. The principal outcome measure was the Yale-Brown Obsessive-Compulsive Scale. Results: All treatments significantly reduced general OCD severity and specific symptom dimensions without a significant difference between treatments. I-CBT was associated with significant reductions in all symptom dimensions at post-test. Also, I-CBT led to significantly greater improvement in overvalued ideation, as well as significantly higher rates of remission as compared to MBSR at mid-test. Conclusions: I-CBT and MBSR appear to be effective, alternative treatment options for those with OCD that yield similar outcomes as A-CBT. I-CBT may have an edge in terms of the rapidity by which patients reach remission, its generalizability across symptom dimension, its potentially higher level of acceptability, and effectiveness for overvalued ideation. Future research is needed to assess whether additional alternative treatments options can help to increase the number of people successfully treated.

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Published by S. Karger AG, Basel

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Inference-Based Cognitive-Behavioral Therapy for OCD

Introduction

Obsessive-compulsive disorder (OCD) is a serious mental health problem characterized by obsessional thoughts and time-consuming compulsive rituals [1]. The psychological treatment of choice is cognitive-behavior therapy (CBT), either alone or with pharmacotherapy [2]. CBT-as-usual involves principally the administration of exposure and response prevention (ERP) with the possible addition of cognitive interventions. ERP involves deliberate and prolonged behavioral (or mental) exposure to the feared object (or thought) combined with prevention of rituals or safety behaviors [3]. Cognitive interventions may be added to this approach which are typically based on appraisal models of OCD [4].

Appraisal-based models of OCD claim that intrusive cognitions transform into obsessions due to maladaptive appraisals and dysfunctional beliefs, which engender distress and compulsive actions [5]. A number of obsessive beliefs or trait-like constructs have been proposed to underlie the dysfunctional appraisal of intrusive cognitions [6, 7], although research into their specificity to OCD has been mixed, leading some to question their role in its pathogenesis [8]. Nonetheless, appraisal-based cognitive-behavioral therapy (A-CBT) is one of the most commonly practiced forms of CBT with modification of appraisals about the significance of intrusive thoughts as its central cognitive component and varying elements of ERP as its behavioral component [9].

Meta-analyses indicate that the majority of patients benefit from CBT [10–12], although residual symptoms typically remain [13]. There are also subgroups of patients, especially those with overvalued ideas, who do not seem to benefit to the same extent as others [14, 15]. Further, ERP is often a central treatment component, which has been associated with low treatment acceptability [16], lower suitability for specific subtypes [9], and high levels of treatment refusal and dropout [17]. Finally, despite attempts to improve outcomes with appraisal-based cognitive interventions, there is no evidence of any benefit in doing so [10–12].

An alternative approach, termed the inference-based approach, represents a continuation of historical thinking that considers pathological doubt to be the central problem in OCD [18–20]. This approach argues that obsessions are faulty inferences of doubt (e.g., “I might have forgotten to lock the door”; “I might hurt someone”), which are a separate sphere of influence from appraisals that occur after the initial doubt or intrusion [21, 22]. Indeed, the manifestation of doubt is increasingly viewed as a central feature of OCD, with doubt being the most commonly reported intrusion [23], which exerts the strongest influence over other symptom dimensions [24].

According to the inference-based approach, the dysfunctional reasoning process giving rise to obsessional doubts is characterized by an overreliance on the imagination or possibilities that are not based on direct evidence or sensory input from the immediate environment, both internal and external [19]. This reasoning process is termed “inferential confusion” [25, 26], which is related to symptoms of OCD independent from obsessive beliefs, appraisals and mood states [27–29] and linked to successful treatment outcomes [30]. Consequently, inference-based cognitive-behavioral therapy (I-CBT) primarily focuses on the reasoning underlying obsessional doubt instead of appraisals and behaviors that might follow from these thoughts [31, 32]. These different emphases of I-CBT and A-CBT have previously been referred to as an “upstream” versus “downstream” focus in the obsessional sequence [33].

There is evidence for the effectiveness of I-CBT with an early small-scale RCT showing a similar outcome in comparison to A-CBT and ERP [34]. This result was confirmed in a larger RCT among patients with limited insight, which found that I-CBT was as effective as A-CBT but more effective among a subgroup of patients with high levels of overvalued ideation [15]. In addition, a previous open trial found that I-CBT is effective across all major symptom dimensions of OCD, as well as treatment-resistant groups [30]. It therefore is unlikely that I-CBT significantly outperforms A-CBT in general, but it may be more effective for certain subgroups and specific symptom dimensions.

The principal aim of the current multicenter RCT was to provide further evidence for the effectiveness of I-CBT as a viable and alternative evidence-based cognitive-behavioral treatment through a comparison with A-CBT and an adapted mindfulness-based stress reduction (MBSR) intervention. MBSR is used across a range of conditions to assist people to deal better with stress, pain, anxiety, and depression [35], with preliminary evidence for its effectiveness in treating symptoms of OCD [36–38]. Consequently, A-CBT served as a specialized cognitive-behavioral comparison condition to I-CBT, while MBSR served as a non-specific active control condition to both. We hypothesized that all three treatment modalities would be effective in reducing symptom severity, but that I-CBT would be superior in its impact across specific symptom dimensions of OCD as compared to the other treatments.
Materials and Methods

Study Design
The current study is a parallel-group multisite RCT comparing the outcome of three psychotherapeutic treatments (I-CBT, A-CBT, and MBSR) in a sample of OCD patients with a 6-month follow-up (ClinicalTrials.gov identifier, NCT01794156). Participants were randomized to each treatment condition following baseline interviews using a computerized random number generator with a ratio of 1:1:1. The allocation sequence was kept concealed from the independent evaluators and therapists. The trained evaluators were kept blind to treatment assignment throughout the trial (baseline, mid-test, post-test, and follow-up) and had no special interest in the study’s outcome.

Participants and Procedures
The trial enrolled participants at two sites, the Montreal Mental Health University Institute affiliated with the University of Montreal and the Cyberpsychology Lab of the University of Quebec in Outaouais, between September 2012 to August 2019. Diagnosis of OCD was established with the Structured Clinical Interview for DSM-IV [39]. Patients aged 18–65 were eligible to partake if they met the following criteria: (1) a primary diagnosis of OCD according to DSM-IV; (2) no other principal axis I disorder requiring treatment first; (3) no evidence of current suicidal intent or substance abuse; (4) no evidence of past or current schizophrenia, bipolar or neurocognitive disorder; (5) no change in medication type or dose during the 12 weeks before treatment (4 weeks for anxiotics).

After randomization, participants were assigned to a trained therapist in one of the three treatments (I-CBT, A-CBT, and MBSR). All therapists (n = 15) met the requirements of the provincial licensing body to provide psychotherapy at the doctoral level or as licensed psychologists and were intensively trained in adherence to protocol. Each therapist provided only one type of treatment and received regular supervision from a senior clinical psychologist. All treatment sessions were audiorecorded for supervision and to establish treatment integrity as assessed by independent raters on level of compliance with treatment protocol using a 4-point scale (range = 0–3).

Treatment Interventions
Conditions of treatment delivery, duration, and monitoring were equivalent across treatment modalities. Treatments were delivered in 26 weekly, 1-h, face-to-face meetings with four initial sessions for individual case formulation and treatment planning, followed by 22 treatment sessions in accordance with manuals made available to therapists for each treatment intervention (online suppl. material for detailed descriptions of the treatments; see www.karger.com/doi/10.1159/000524425 for all online suppl. material).

Appraisal-Based Cognitive-Behavior Therapy
A-CBT consisted of ERP combined with cognitive interventions focused on correcting maladaptive beliefs and thoughts related to the dysfunctional appraisal of intrusive cognitions [40]. Treatment initially focused on the normalization of intrusive thoughts and the role of maladaptive appraisals and dysfunctional beliefs maintaining symptoms of OCD [6, 7]. Next, clients were trained to identify and challenge their key beliefs using formal cognitive restructuring methods. This correction led to the second phase of treatment with deliberate and prolonged ERP [41] combined with behavioral experiments to help the client discover that their fears are unfounded (i.e., “hypothesis testing”) [9]. ERP exercises were carried out both within and between sessions as homework assignments using imaginal and in vivo exposure with the prevention of overt and covert compulsions according to hierarchies.

Adapted Mindfulness-Based Stress Reduction
The MBSR intervention was based on the curriculum developed by Santorelli and Kabat-Zinn [35] with adaptations for length and structure for its delivery in an individual format in a clinical setting [37, 42]. Treatment commenced with experiential training and skill development concerning the role of perception and other mental factors in the assessment of stress and the pivotal role of self-responsibility in the positive development changes in health-enhancing behaviors. Participants were trained in formal mindfulness practices (body scan, mindful movement, and sitting meditations) and encouraged to apply mindfulness skills to everyday activities and real-life stressful situations. The experiential practice of skills was carried out, emphasizing more rapid recovery from stressful encounters and using cognitive awareness to interrupt and intervene in habitual behaviors and choose more effective responses.

Inference-Based Cognitive-Behavior Therapy
I-CBT consisted of cognitive interventions focused on dysfunctional reasoning to bring resolution to the obsessional doubt [31, 32]. During treatment, patients are taught that obsessional doubt is generated on an imaginary basis without any direct evidence to support it. Further, the reasoning distortions in idiosyncratic reasoning narratives justifying obsessional doubts are identified, and an alternative, more reality-based narrative is developed with the patient. Finally, the selective nature of obsessional doubt is undermined, and the client educated in the thematic nature of the obsessional doubt as it is dictated by their vulnerable or feared self. The end-stage of treatment consists of “reality sensing” by encouraging the patient to act upon the knowledge that the obsessional doubt is incorrect while trusting their senses with self-confidence without putting in any additional unnecessary effort.

Outcomes
Demographic (age, gender, education, marital status) and clinical variables were collected at baseline. All outcome measures were administered at baseline, post-test, and follow-up (6 months after post-test). The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) [43] served as the principal outcome measure and was administered at baseline, mid-test (at the 11th treatment session), post-test, and follow-up (6 months after post-test). The YBOCS is the instrument of choice for clinician assessment of OC severity independent from any specific symptom dimension. The Vancouver Obsessive-Compulsive Inventory (VOCI) [44] served as a secondary outcome measure. Only the most common and well-established symptom dimensions as measured by the VOCI were considered, which include the subscales obsessions, contamination, checking, and “just right” [45]. In addition, several secondary key endpoints related to non-specific symptoms, general functioning and overvalued ideation were identified. Non-specific secondary outcome measures were the Beck Anxiety Inventory [46] and the

DOI: 10.1159/000524425

Psychother Psychosom 2022;91:348–359

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Beck Depression Inventory [47]. Clinician-rated secondary outcome measures included the Current Functioning Assessment (CFA) [48] and the Overvalued Ideation Scale (OVIS) [49]. Dichotomous secondary outcome measures with cut-off points based on international consensus among experts in the field of OCD [50] were: (a) treatment response status, as defined by a decrease on the YBOCS between pre- and post-test of at least 35%, (b) remission status, as defined by a YBOCS post score ≤12, (c) relapse status, as defined by no longer meeting criteria for treatment response or remission at follow-up in comparison to treatment status established at post-test, and (d) treatment refusal and dropout rates.

### Sample Size

For our first hypothesis that all three treatments would be effective in reducing symptoms, power analyses indicated a required sample size of 37 in each treatment for a total of 112 participants to detect small to medium effect sizes with a power of 95% and four repetitions with correction for multiple comparisons (1-β% = 0.95, α = 0.01, Cohen’s f = 0.20). For our second hypothesis regarding differences between treatments on specific symptom dimensions, power analyses indicated a required sample size of 94 participants to detect differences with a medium effect size between treatments with three repetitions (1-β% = 0.80, α = 0.01, Cohen’s f = 0.25).

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**Fig. 1.** Flow diagram of a randomized controlled trial comparing inference-based cognitive-behavioral therapy (I-CBT), appraisal-based cognitive-behavioral therapy (A-CBT) and mindfulness-based stress reduction (MBSR) training.
Statistical Analysis

Unless specified otherwise, analyses were run on the intent-to-treat (ITT) sample. Differences between groups and treatment sites on demographic and clinical variables at baseline were calculated using one-way ANOVA for continuous variables and χ² statistics for categorical variables. A linear mixed model (LMM) was used to test treatment effects within- and between variables on the outcome measures. Bonferroni correction was applied to each family of measures (OCD symptom measures, p < 0.01; non-specific symptom measures, p < 0.0125; measures of clinical significance, < 0.025). Treatment conditions, time points, and interactions were entered as fixed effects in the model with a restricted maximum likelihood algorithm to estimate means. Site differences concerning outcomes were also investigated with LMM with treatment site entered as an additional fixed factor. Differences in response and remission rates were investigated with generalized linear models with logit link function and binomial variance function specified for dichotomous variables. Differences in rates of treatment refusal and dropout between treatment conditions were calculated with Fisher’s exact tests with Freeman and Halton’s extension [51] to account for the 2 × 3 contingency table.

Results

As shown in Figure 1, we assessed 163 individuals for study eligibility. Of these, 33 did not meet entry criteria, and another 19 declined to participate, resulting in 111 individuals in the ITT sample randomized to one of the three treatments, 38 participants I-CBT, 39 A-CBT, and 34 MBSR. After randomization, 8 refused treatment, and another 22 dropped out of treatment, resulting in a total of 81 individuals that completed treatment (the per-protocol sample at post-test).

Baseline Characteristics and Differences

At baseline, participants had a mean score of 25.51 (SD = 6.15) on the YBOCS, reflecting severe OCD symptoms. Baseline levels of symptomatology in specific symptom dimensions, as measured by the VOCI, were similar to those previously reported among OCD patients [44] with a mean score of 11.17 (SD = 9.15) for

| Characteristics | A-CBT (n = 39) | I-CBT (n = 38) | MBSR (n = 34) | p |
|-----------------|---------------|---------------|--------------|---|
| Demographics    |               |               |              |   |
| Age             | 36.9±12.8     | 40.4±13.4     | 39.7±13.0    | 0.52 |
| Education, % university degree | 18 (46.2%) | 14 (36.8%) | 15 (44.11%) | 0.91 |
| Sex, % women    | 18 (46.2%)    | 24 (63.2%)    | 21 (61.8%)   | 0.27 |
| Occupation, % working full time | 16 (41.0%) | 15 (39.5%) | 19 (55.9%) | 0.47 |
| Marital status, % married/cohab. | 16 (41.0%) | 14 (36.8%) | 14 (41.17%) | 0.96 |
| OCD severity    |               |               |              |   |
| Overall severity (YBOCS) | 25.9±5.2 25.3±6.8 25.5±6.5 | 0.94 |
| Contamination (VOCI) | 14.9±13.4 22.0±12.6 20.6±13.3 | 0.04 |
| Checking (VOCI)  | 9.9±8.0       | 13.4±6.8      | 12.6±7.8     | 0.06 |
| Obsessions (VOCI) | 11.4±10.5 10.8±8.5 11.1±8.2 | 0.97 |
| Just right (VOCI) | 19.8±10.4 21.0±9.6 25.4±11.2 | 0.11 |
| Secondary outcomes |               |               |              |   |
| Overvalued ideation (OVIS) | 5.3±1.7 5.4±1.5 5.0±1.6 | 0.55 |
| Depression (BDI) | 16.9±13.4 20.0±12.6 16.7±12.0 | 0.46 |
| Anxiety (BAI)    | 16.2±12.4     | 16.1±11.8     | 19.8±12.3    | 0.35 |
| Functioning (CFA) | 5.0±1.6 5.2±1.9 5.2±1.6 | 0.92 |
| Comorbidity and medication |               |               |              |   |
| Current comorbidity, % yes | 15 (38.5%) 16 (42.1%) 14 (41.2%) | 0.94 |
| Antidepressants, % yes | 12 (30.8%) 20 (52.6%) 17 (50.0%) | 0.65 |
| Benzodiazepine, % yes | 5 (12.8%) 5 (13.2%) 3 (8.8%) | 0.76 |
| Atypical antipsychotics, % yes | 5 (12.8%) 4 (10.5%) 3 (8.8%) | 0.84 |

Values represent means ± SD or n (%). YBOCS, Yale-Brown Obsessive Compulsive Scale; VOCI, Vancouver Obsessive Compulsive Inventory; OVIS, Overvalued Ideation Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; CFA, Current Functioning Assessment; A-CBT, appraisal-based cognitive-behavioral therapy; I-CBT, inference-based cognitive-behavioral therapy; MBSR, mindfulness-based stress reduction.
### Table 2. OCD symptom outcome measures within treatment conditions and by treatment

| Variables | Appraisal-based CBT (n = 39) | Inference-based CBT (n = 38) | Mindfulness-based stress reduction (n = 34) |
|-----------|-----------------------------|-------------------------------|------------------------------------------|
|           | EMM 95% CI comparison with pretest | EMM 95% CI comparison with pretest | EMM 95% CI comparison with pretest |
|           | t p d | t p d | t p d |
| OCD severity (YBOCS) | | | |
| Pretest    | 25.86 23.81–27.92 | 25.33 23.33–27.34 | 25.47 23.34–27.60 |
| Midtest    | 18.23 15.95–20.51 | 15.65 13.32–17.97 | 18.06 15.71–20.41 |
| Posttest   | 13.40 10.21–16.59 | 13.75 10.62–16.88 | 15.05 11.76–18.34 |
| Follow-up  | 11.65 8.21–15.08 | 11.27 7.88–14.66 | 12.40 9.12–15.68 |
| Contamination (VOCI) | | | |
| Pretest    | 14.91 10.54–19.29 | 22.00 17.31–26.65 | 20.59 15.42–25.75 |
| Posttest   | 12.34 9.42–15.25 | 15.83 12.50–19.17 | 17.98 14.62–21.33 |
| Follow-up  | 10.78 6.15–15.40 | 16.67 11.71–21.63 | 16.00 11.53–20.47 |
| Checking (VOCI) | | | |
| Pretest    | 9.86 7.34–12.39 | 13.95 11.20–16.63 | 12.56 9.56–15.55 |
| Posttest   | 6.26 4.09–8.42 | 8.01 5.59–10.43 | 10.37 7.85–12.88 |
| Follow-up  | 7.48 4.59–10.37 | 8.82 5.69–11.95 | 7.47 4.43–10.50 |
| Obsessions (VOCI) | | | |
| Pretest    | 11.37 8.30–14.44 | 10.75 7.47–14.02 | 11.08 7.47–14.69 |
| Posttest   | 10.43 7.79–13.07 | 6.82 3.86–9.78 | 9.01 5.96–12.07 |
| Follow-up  | 9.22 5.91–12.53 | 6.71 3.11–10.30 | 6.05 3.11–10.30 |
| Just Right (VOCI) | | | |
| Pretest    | 19.80 16.38–23.23 | 21.03 17.36–24.70 | 25.44 21.39–29.49 |
| Posttest   | 15.83 12.72–18.94 | 15.10 11.57–18.62 | 18.99 15.40–22.58 |
| Follow-up  | 14.00 9.21–18.78 | 14.75 9.62–19.87 | 16.17 11.57–20.78 |

YBOCS, Yale-Brown Obsessive Compulsive Scale; VOCI, Vancouver Obsessive-Compulsive Inventory; A-CBT, appraisal-based cognitive-behavioral therapy; I-CBT, inference-based cognitive-behavioral therapy; MBSR, mindfulness-based stress reduction. Significance level threshold <0.01. *Treatment effect within the treatment condition. **Comparison of treatment effect between the conditions.
Table 3. Non-specific symptom measures within treatment conditions and by treatment

| Variables          | Appraisal-based CBT (n = 39) | Inference-based CBT (n = 38) | comparison with A-CBT | comparison with MBSR | Mindfulness-based stress reduction (n = 34) |
|--------------------|------------------------------|-----------------------------|----------------------|----------------------|-------------------------------------------|
|                    | EMM 95% CI comparison with   | EMM 95% CI comparison with  | t p d                | t p d                | EMM 95% CI comparison with pretest         |
|                    | pretesta                    | A-CBT                      |                      |                      |                                          |
| Overvalued ideation (OVIS) |     |                             |                      |                      |                                          |
| Pretest            | 5.00 4.47–5.54 5.25 4.72–5.78 | 6.69 <0.001 1.55 1.04 0.34 | 2.80 <0.01 0.66 3.87 3.23–4.51 | 2.64 <0.01 0.63 3.60 0.001 0.86 4.15–41.5 3.08 <0.001 1.21 0.36 0.72–0.08 |
| Midtest            | 5.14 2.52–3.77 6.69 <0.001 1.55 1.04 0.34 | 2.80 <0.01 0.66 3.87 3.23–4.51 | 2.64 <0.01 0.63 3.60 0.001 0.86 4.15–41.5 3.08 <0.001 1.21 0.36 0.72–0.08 |
| Posttest           | 3.90 2.24–3.55 7.16 <0.001 1.66 1.17 0.25 0.27 2.27 0.03 0.54 3.46 2.76–4.15 1.95–3.52 5.08 <0.001 1.21 0.36 0.72–0.08 |
| Follow-up          | 2.81 2.04–3.59 5.65 <0.001 1.28 0.23 0.82 0.05 0.58 0.57 0.14 2.73 2.05–3.42 1.95–3.52 5.08 <0.001 1.21 0.36 0.72–0.08 |
| Depression (BDI)   |                              |                             |                      |                      |                                          |
| Pretest            | 16.91 12.83–20.99 19.96 15.88–24.04 | 3.03 <0.01 0.75 0.71 0.48 0.17 11.28 6.43–16.14 2.22 0.03 0.55 12.19 2.95 <0.01 0.73 0.23 0.82–0.05 |
| Posttest           | 10.34 5.92–14.78 12.15 7.48–16.81 3.33 <0.01 0.75 0.71 0.48 0.17 11.28 6.43–16.14 2.22 0.03 0.55 12.19 2.95 <0.01 0.73 0.23 0.82–0.05 |
| Follow-up          | 9.68 5.30–14.07 9.57 4.90–14.23 4.45 <0.001 1.01 0.99 0.33 0.22 1.20 0.23 0.28 10.19 7.66–14.62 2.95 <0.01 0.73 0.23 0.82–0.05 |
| Anxiety (BAI)      |                              |                             |                      |                      |                                          |
| Pretest            | 16.01 12.08–19.95 16.02 12.06–19.98 | 3.36 <0.001 0.86 0.18 0.86 0.04 –0.17 0.86 –0.04 12.24 8.45–16.02 3.97 <0.001 0.96 0.35 0.73 0.08 |
| Posttest           | 9.36 5.84–12.87 8.92 5.19–12.62 3.80 0.001 0.87 0.18 0.86 0.04 –0.17 0.86 –0.04 12.24 8.45–16.02 3.97 <0.001 0.96 0.35 0.73 0.08 |
| Follow-up          | 6.54 2.62–10.45 4.87 <0.001 1.12 0.79 <0.001 1.12 0.09 0.93 0.02 –0.53 0.60 0.13 9.07 5.25–12.88 5.67 <0.001 1.38 0.46 0.65 0.11 |
| Functioning (CFA)  |                              |                             |                      |                      |                                          |
| Pretest            | 5.18 4.60–5.76 5.06 4.48–5.64 4.32 3.75–4.89 4.54 <0.001 1.06 1.23 0.22 0.29 0.13 0.90 0.03 3.87 3.27–4.47 4.41 <0.001 1.10 1.11 0.27 0.27 |
| Midtest            | 4.32 3.75–4.89 3.68 3.08–4.29 4.54 <0.001 1.06 1.23 0.22 0.29 0.13 0.90 0.03 3.87 3.27–4.47 4.41 <0.001 1.10 1.11 0.27 0.27 |
| Posttest           | 2.98 2.28–3.64 6.35 <0.001 1.50 3.24 2.53–3.94 5.18 <0.001 1.20 –0.77 0.45 –0.18 –0.31 0.76 –0.07 3.21 2.49–3.93 5.45 <0.001 1.36 0.45 0.66 –0.11 |
| Follow-up          | 2.41 1.67–3.14 7.55 <0.001 1.78 2.77 1.95–3.59 5.59 <0.001 1.30 –0.88 0.39 –0.21 –0.60 0.55 –0.15 2.57 1.84–3.30 7.19 <0.001 1.80 0.29 0.77 –0.07 |

OVIS, Overvalued Ideation Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; CFA, Current Functioning Assessment; A-CBT, appraisal-based cognitive-behavioral therapy; I-CBT, inference-based cognitive-behavioral therapy; MBSR, mindfulness-based stress reduction. Significance level threshold <0.0125. *Treatment effect within the treatment condition. **Comparison of treatment effect between the conditions.
obsessions, 11.94 (SD = 9.15) for checking, 19.24 (SD = 13.47) for contamination, and 21.82 (SD = 10.51) for “just right” symptoms. Baseline levels of depression (mean = 17.89; SD = 12.68) and anxiety (mean = 17.29; SD = 12.16) indicated moderate levels of symptomatology. Baseline level of overvalued ideation as measured by the OVIS was 4.96 (SD = 1.60). Patients experienced significant levels of interference in their daily functioning as established by the CFA (mean = 5.10; SD = 1.68). At least one DSM-IV comorbid psychiatric disorder was diagnosed in 40.6% of patients. At the time of study entry, 47.1% of patients received anti-depressants, 11.5% benzodiazepines, and 10.3% atypical antipsychotics. All patients remained on the same medication at the same dosage throughout the trial.

Table 1 shows the demographics, baseline scores, and clinical characteristics of the study sample by treatment group. There were no significant differences between the treatment groups except for the contamination subscale of the VOCI. We randomly selected 1 in 10 patient recording sets in each treatment group to establish treatment integrity. There were no significant differences in compliance between the treatments, with an average compliance score of 2.7 (SD = 0.5) for I-CBT, 2.62 (SD = 0.5) for A-CBT, and 2.67 (SD = 0.9) for MBSR. We also compared differences at baseline between the two recruitment sites (Montreal/Gatineau), which revealed no significant differences. In addition, a comparison of the per-protocol sample with dropouts showed no significant differences in the pre-test variables.

**OCD Symptom Measures**

LMM showed significant reductions in our primary outcome YBOCS in each of the treatments. At post-test, YBOCs scores significantly decreased for I-CBT [estimated mean = −11.45 (95% CI = −14.6 to −8.4), t(83.98) = −7.34, p < 0.001], A-CBT [estimated mean = −11.72 (95% CI = −14.8 to −8.6), t(85.03) = −7.49, p < 0.001] and MBSR [estimated mean = −10.20 (95% CI = −13.4 to −7.0), t(89.18) = −6.26, p < 0.001]. Table 2 presents YBOCS scores at mid-test, post-test, and follow-up as compared to pre-test within each treatment modality and comparison of treatments conditions at each time point. There was no significant time by treatment condition effect at any of the time-points for the YBOCS. Per-protocol analyses confirmed the findings of the ITT analyses. Finally, LMM with treatment site entered as an additional fixed factor showed no significant main and interaction effects [Site: F(1, 97.744) = 1.698, p = 0.20; Time*Site: F(2, 75.173) = 2.550, p = 0.09;
Time*Modality*Time: F(6, 85.642) = 0.656, p = 0.69]

LMM also showed significant reductions in specific OCD symptom dimensions. At post-test, I-CBT significantly improved all symptom dimensions. A-CBT significantly improved checking and “just right” symptoms, whereas MBSR significantly improved “just right” symptoms. However, between-treatment comparisons revealed no significant difference for any of the specific symptom dimensions at post-test. Additionally, no significant differences between sites in treatment effects on the VOCI subscales were found.

Non-Specific Outcome Measures
All treatments showed significant improvements in overvalued ideation, depression, anxiety and functioning (see Table 3). There were no significant differences between treatments for depression, anxiety, and functioning. However, I-CBT was significantly more effective in reducing overvalued ideation compared to MBSR at mid-test.

Measures of Clinical Significance
Dichotomous secondary outcomes of treatment response and remission are represented in Table 4. At mid-test, MBSR had significantly lower remission rates than I-CBT (8.3 vs. 42.0%). There were no significant differences in treatment response and remission rates between treatments at post-test and follow-up. One patient in each treatment arm experienced deterioration during treatment with a higher score on the Y-BOCS at post-test as compared to pre-test. Two patients (5.1%) in I-CBT, two (5.2%) in A-CBT and one (2.9%) in MBSR relapsed during the 6-month follow-up period.

Treatment Refusal and Dropout
We compared treatment refusal (I-CBT = 5.2%; A-CBT = 2.6%; MBSR = 14.3%) and dropout rates (I-CBT = 18.4%; A-BCT = 25.6%; MBSR = 14.7%) across the treatment conditions and found no significant differences (p = 0.15 for treatment refusal; p = 0.55 for dropout, and p = 0.69 for combined rates).

Discussion
All treatments were effective in reducing OCD symptom severity without any significant differences between treatments. Most patients responded to treatment (48.2–64.3%), and a substantial portion reached remission (35.3–53.5%) with no significant differences between treatments at post-test and follow-up. However, at mid-test, remission rates with I-CBT were significantly higher than with MBSR, indicating that I-CBT worked faster. Similarly, I-CBT was significantly more effective than MBSR in reducing levels of overvalued ideation at mid-treatment. Previous research has found that I-CBT is particularly effective among subgroups with high levels of overvalued ideation given its conceptualization of OCD as a belief disorder [15, 34]. However, research findings on the effectiveness of I-CBT in specific subgroups are still preliminary, and further research is needed to identify predictors of non-response and subgroups that might benefit from alternative treatments [52].

Given previous findings, no significant difference in reducing overall symptom severity was expected [15, 30, 34]. However, it was hypothesized that I-CBT would be more effective across specific symptom dimensions of OCD given varying treatment rationales and ingredients (see online suppl. material). Specific to I-CBT is a focus on the dysfunctional reasoning process (i.e., inferential confusion) hypothesized to underlie the occurrence of pathological doubts (i.e., obsessions) regardless of symptom subtype [19]. In A-CBT, the focus is on altering appraisals of significance given that the model holds that obsessions develop from what are otherwise normal, intrusive thoughts. MBSR is a non-OCD specific meditative intervention that aims to foster and promote the cultivation of conscious awareness of present moment experiences (i.e., thoughts, feelings, and sensations), coupled with an accepting and non-judgmental mindset.

Results showed that I-CBT was associated with significant reductions in all major symptom dimensions, confirming its generalizability across symptoms of OCD [30]. As noted earlier, the strong influence exerted by doubt over other symptom dimensions [23, 24], which is the principal treatment target of I-CBT, might account for its generalizability across symptoms. A-CBT also led to significant reductions in checking and just right symptoms, but not in contamination and obsessions. Indeed, those with unacceptable thoughts have traditionally been considered difficult to treat, and several have argued that ERP is not well-suited for this subtype [9]. Nonetheless, we cannot conclude that I-CBT was superior since there was no significant difference between treatments despite differential patterns within treatments.

One explanation for the finding that the treatments did not differ significantly may, to some extent, be related...
to common factors that exist across most psychotherapies (working alliance, hope, guidance, empathy, structure, etc.); and, especially, to other potential areas of overlap that are clearly different from other forms of psychotherapy, yet common among CBT-related treatments (e.g., avoidance; see OSM for a detailed analysis on areas of overlap). In particular, they all include cognitive interventions that are focused on reducing the intensity and impact of obsessions, while encouraging various forms of exposure or ways of approaching obsessional situations without neutralizing and avoidance, albeit with varying rationales, targets, methods, and techniques. These potential areas of overlap highlight the need for adaptive designs and dismantling studies which may provide valuable information on the unique benefits of specific interventions [53].

To our knowledge, the current study is the first to compare mindfulness training with other treatments in patients with OCD. Clinical trials have evaluated the efficacy of MBSR for a variety of psychological disorders [54]. The current trial showed that MBSR did not significantly differ in outcomes compared to A-CBT for those with OCD. However, it is notable that MBSR only had a significant impact on “just right” symptoms at post-test. This finding is consistent with the focus of mindfulness-based approaches on increasing flexibility towards one’s own thinking and experience [38, 55]. Also, improvement in the other symptom dimensions occurred at follow-up, perhaps suggesting a more delayed, non-specific effect as compared to the other treatments.

The current results do not establish non-inferiority or equivalency, which requires larger sample sizes. Also, given that there was no placebo or wait-list control group, we cannot completely eliminate the possibility of external factors accounting for reductions in symptomatology. However, this seems unlikely since the observed effects sizes are comparable to or in the upper range of those obtained from meta-analyses of trials utilizing CBT ($d = 1.13–1.90$), which differ significantly from placebo or wait-list control conditions ($d = 0.74–1.39$) [11–13, 56, 57]. Therefore, we might conclude that the current results support the use of MBSR and I-CBT as alternative treatments for OCD. Indeed, clinical guidelines that prioritize the use of CBT with ERP over other psychological interventions are questionable given that the different variants of CBT have potential areas of overlap and produce similar outcomes [57]. Also, similar outcomes between treatments do not automatically imply that alternative forms of CBT may not offer additional benefits since different treatments may be differentially effective for different clients [58, 59].

Overall, results suggest that both I-CBT and MBSR are viable and effective cognitive-behavioral treatments, which provide those with OCD with additional evidence-based treatment options. In particular, I-CBT was found to be generalizable across all major symptom dimensions and reach high remission rates within a relatively short amount of time without prolonged and deliberate exposure to fearful stimuli. Future research will need to determine whether these benefits are sufficient to increase the number of people with OCD successfully treated.

Acknowledgement

Dr. Kieron O'Connor passed away on the 27th of August, 2019 in Montreal, Canada. We are grateful for his leadership and many contributions to the field.

Statement of Ethics

The study protocol was reviewed and approved by the research ethics board of the Centre intégral universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal and the Université du Québec en Outaouais [Project No. MP-12-2012-82, MP-IUSMM-2011-020]. All participants provided written informed consent.

Conflict of Interest Statement

The first four authors and the last author have received financial research support from the Canadian Institutes of Health Research to conduct the present study. F.A. has received royalties from treatment manuals on inference-based cognitive-behavioral therapy. M.E.L. has received royalties from treatment manuals on the management of tic and habit disorders. S.B. has received financial research support from the Canada Research Chairs program and Canadian Institutes of Health Research during the conduct of this study. D.K. has received financial support from the Institute du Savoir Montfort Hospital, Ontario Mental Health Foundation, and Canadian Institutes of Health Research during the conduct of this study. The other authors report no financial relationships with commercial interests related to the present study.

Funding Sources

The current research was supported by a grant from the Canadian Institutes of Health Research (grant No. 114995). The funding source had no role in design, data collection, analyses, interpretation and the reporting of findings.
Author Contributions

All authors have substantially contributed to the current study, including conception and design or analysis and interpretation of data. In addition, each of the authors contributed to the initial draft of the article or provided critical revisions for its intellectual content.

Data Availability Statement

The data that support the findings of this study are not publicly available due to ethics restrictions, but available from the corresponding author (F.A.) upon reasonable request with individual permission from the local institution ethics board.

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