Dr. Xiu-Xia Song

Vice Director, Editorial Office

Word Journal of Psychiatry

Manuscript No.: 29067
Title: Cognitive-behavioural therapy for obsessive-compulsive disorder co-occurring with psychosis: systematic review of evidence

Dear Dr. Xiu-Xia Song,
We appreciate the time and effort of the reviewer for his/her thoughtful feedback.
Answers to the reviewer's comment are listed point by point below in boldface.
We hope that we have addressed adequately all the issues raised.
Please feel free to contact me with any additional questions or comments on this paper.
I look forward to your final decision about the paper.

Antonio Tundo, MD

Referee #1

This is a generally well-written, timely and successful qualitative overview on CBT treatment experiences of OCS/OCD in schizophrenia. In my view, some points need clarification and revision:

Major points:

1. The description of CBT (how? how long? modifications in patients with psychosis? etc.) and treatment effects (neuropsychological and psychological/psychopathological domains, more details on Y-BOCS etc. score changes if available, rather than "global functioning") is a bit superficial.

We acknowledged the reviewer's suggestion to reported more details on Y-BOCS, GAF e CGI-S score changes and on CBT approaches modifications described in the case series study.

The CBT duration was already reported for case reports as well as for case series in Table 1.

The reviewed studies did not analyse the effects of CBT on neuropsychological and psychological/psychopathological domains, except for Tundo et al. study, in which the authors examined the effects of CBT on OC severity using the YBOCS and overall severity of illness, using the CGI.

2. Is there a reason to distinguish between "ritual" and "response" prevention? If so, please clarify; if not, "CBT/ERP" should be used throughout the paper (if appropriate).

At the end of the introduction, we had already specified that the acronym CBT stands for "cognitive-behavioral therapy incorporating exposure and ritual prevention". We acknowledged the suggestion of the reviewer and used CBT throughout.

3. Similarly: OCD (as a clearly diagnosed disorder according to DSM or ICD) is rarely diagnosed properly in patients with schizophrenia; OCS are probably much more prevalent in clinical and research settings. I recommend to use OCS/OCD throughout (incl. title).

We acknowledged the suggestion of the reviewer and

a) **In Introduction we specified separately the prevalence of OCS and OCD in patients with SCH according to Swets et al., 2014 (new reference 1)**

b) **we changed OCD to OCS or OCS/OCD in the text and in the abstract when appropriate**

c) **all patients included in the reviewed papers fulfill the criteria for OCD, so changing the title in our opinion would be misleading**

4. INTRO: other available non-pharmacological and psychotherapeutic treatment options for OCS/SCH should be briefly summarized (ECT; rTMS, DBS, ..., Psychodynamic Therapy...)

We acknowledged the suggestion of the reviewer and we reported in the Discussion that ECT, rTMS, DBS, Psychodynamic Therapy are further potential options in treatment- resistant patients.

5. The interpretation of the influence of antipsychotics on OCD/OCS in SCH/SAD should be more cautious througout; only for clozapine (and probably for olanzapine) there is some evidence that OCS occur at a higher frequency compared to the natural illness course. OCS can occur or get worse also under no treatment or treatmetn with a FGA or other SGAs (which could be not primarily 5HT2-R-antagonistic) (see, e.g, Scheltema Beduin et al. 2012, J Clin Psychiatry); maybe a model assuming an interaction between genetic/biological predispositions, life-time conditioning, and treatments, is most appropriate.

We acknowledged the suggestion of the reviewer, we changed the text (Introduction) and the Abstract, and included the suggested reference in the appropriate place

6. The interpretation of potential effects, effect sizes, and predictors of CBT in patients with SCH+OCS should be more cautious because the really low number of published treatment cases, the low methodological quality of reports, and - most important - the obvious lack of control groups or control treatments (TAU...). All effects could finally be due to the natural course of disorders or non-specific therapeutic factors.

We acknowledged the suggestion of the reviewer and we changed the text (Discussion) and the Abstract

Minor points:

7. recent references should be included and discussed; e.g., Leung & Palmer 2016; Rosli et al., 2015; Grover et al. 2015; Schirmbeck et al. 2015; Fonseka et al., 2014; Gahr et al. 2014; Zink et al. 2014; Doyle et al. 2014.

In response to the reviewer's request we included the suggested references in the appropriate place and discussed them

8. p.4. This paragraph should be improved: ... pharmacokinetic drug interactions: a) e.g. "some antidepressants (fluox, fluvox, parox, venlaf, ...) may increase the plasma concentration of particular antipsychotics (e.g., cloz, ola, ris) by inhibition of hepatic cytochrome P450 isoenzymes (e.g., 1A2, 2D6), and ...

We acknowledged the suggestion of the reviewer and we changed the text (Introduction)

9. p.5. Methods, end: the 9 studies should be briefly characterized (type, n, ...)

We acknowledged the suggestion of the reviewer and we specified the number and type of studies identified (Methods)

10. p.6. 2nd/3rd para: it is unclear, which patients were included in the "LOCF" analysis (last paragraph): all 21?, please, clarify.

We acknowledged the suggestion of the reviewer and we specified in the text that all 21 patients were included in the statistical analysis

11. p.7, 3.2. 2nd para, ... and it is consistent ... this sentence needs rephrasing.

We acknowledged the suggestion of the reviewer and we rephrased the sentence

12. p.9. 1st para: ... could be an adverse effect of serotonergic antagonist ... should be stated more cautiously

We acknowledged the suggestion of the reviewer and we rephrasing the sentence more cautionally

13. p.9. last paragraph: the lack of any control group should be mentioned (not only lack of randomization).

We acknowledged the suggestion of the reviewer and we better underlined in the Discussion the lack of a control group or control treatments

14. typing errors/style e.g.

p.3 a so-called schizo-obsessive disroder...;

We acknowledged the suggestion of the reviewer and we corrected the test

p4. interactions: b) ... limit its use in elderly patients and in those treated...

We acknowledged the suggestion of the reviewer and we corrected the test

p.4. dosage of the antipsychotic; ...

We acknowledged the suggestion of the reviewer and we corrected the test

p.5 ritual/response prevention (ERP)

We acknowledged the suggestion of the reviewer and we corrected the test

p.5. Material and Methods ... OCD or OCS...

a) **As previous reported (Major points, n° 3) all patients included in the reviewed papers fulfill the criteria for OCD, so the proposed change in our opinion would be misleading**

b) p.8, line 2 (0% vs. 68%, respectively)

We acknowledged the suggestion of the reviewer and we corrected the test

p.8. The authors...

We acknowledged the suggestion of the reviewer and we corrected the typing error

Kind regards!

Referee #2

Excellent systematic review of CBT for OCD with psychosis.

Referee #3

This is, in summary, a detailed review aimed to review available evidence on the use of cognitive-behavioural therapy (CBT) for treating obsessive-compulsive disorder (OCD) co-occurring with both schizophrenia or schizoaffective disorder (SCH/SA). The manuscript is interesting and well-written as presented; thus, only minor changes are needed in its current version. The authors may find as follows my main comments/suggestions.

1. First, when throughout the Methods section, the authors reported that this is a systematic review of papers focusing on CBT treatment of OCD co-occurring with SCH/SA. I suggest to revise this statement (as well as the title of the paper) and report that this is a detailed and comprehensive review of the current literature upon the proposed main topic. Conersely, systematic reviews generally include specific selection criteria and quality assessment (e.g., PRISMA statement for reporting systematic reviews, a literature search in various existing databases such as Excerpta Medica, Scopus, ScienceDirect, PsycLit, PsycInfo, and Index Medicus search search, an initial examination of all the citations of the obtained studies by at least two reviewers independently, a detailed discussion with the senior author who also independently assessed all the articles and categorized them according to the major areas of interest identified by the reviewers occurred in the case of any disagreement, etc.).

We acknowledged the suggestion of the reviewer and we changed the title, the abstract and the text

2. Furthermore, the authors indicated that they found a total of 9 studies; however, how many articles were screened, selected, and finally included in the present manuscript may be specified.

   We acknowledged the suggestion of the reviewer and we better specified the selection criteria of the papers in Methods

3. Also, while the authors stated that they found a total of 9 studies, Table 1 included only 8 studies. Here, more details/information may be added for the general readership.

   We acknowledged the suggestion of the reviewer and we specified that "*Table 1 shows the demographic and clinical characteristics and the response to CBT of the 10 patients included in the 8 case reports; characteristics and treatment response in patients included in the case series will be analyzed separately*"

4. Importantly, the Discussion section could further stress the main implications related to the frequent co-occurrence of both obsessive-compulsive symptoms or OCD in clinical practice for patients with SCH/SA as well as the importance of using CBT including ERP for treating obsessive-compulsive symptoms/OCD.

We have now reported in Discussion the frequency and consequences of OCS/OCD-SCH comorbidity and suggested that in patients with OCD-SCH/SA comorbidity CBT including ERP could be a viable alternative to pharmacological treatment with SRI.

5. Finally, among the main limitations/shortcomings of the present paper i would also report that since all the included studies were case-reports, thus, the information regarding the efficacy and tolerability of the use of CBT for treating OCD co- occurring with SCH/SA included in these articles are limited due to their main nature.

We acknowledged the suggestion of the reviewer and we introduced the proposed sentence in the abstract and in the text

Referee #4

This is a nicely written review of a very limited literature. The data are adequately described but I would like to see:

1) something about the role of medications and how these might play a part in management (albeit I accept this is not the focus of the paper)

As the reviewer underlines, the role of medication is not in the focus of the paper. Still, we have now reported in Discussion that pharmacotherapy is the most common treatment in clinical practice and added the reference of a recent paper reviewing this topic

2) something for clinicians to guide how CBT might be adapted for use in this group of patients, and the potential barriers and risks of a CBT approach (eg. cognitive barriers and use of CRT)

We have now reported more details on CBT approach modifications described in the case series study and the possible cognitive barriers to the use of this approach

3) a clearer exposition of the limitations of current research in the area

We have now better specified the limitations of current research in the area (Discussion)

3) directions for future research
We have now improved the final sentence in the paper to include directions for future research