Author’s response to reviews

Title: Cognitive Remediation Therapy (CRT) as a Pretreatment Intervention for Adolescents with Anorexia Nervosa during Medical Hospitalization: A Pilot Randomized Controlled Trial Protocol

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Version: 2 Date: 04 Apr 2018

Author’s response to reviews:

March 3, 2018

To: Susana Dodd

From: C. Alix Timko

Re: PAFS-D-17-00164R1

Cognitive Remediation Therapy (CRT) as a Pretreatment Intervention for Adolescents with Anorexia Nervosa during Medical Hospitalization: A Pilot Randomized Controlled Trial Protocol

We are pleased that the reviewers found our prior revisions satisfactory and were happy to further revise and clarify the aforementioned manuscript. We have addressed the reviewers’ and editor’s comments below. The comment is noted in bold and our response follows. The changes made to the manuscript are approved by my co-authors. We are happy to further clarify or make any other additional efforts.

Sincerely,

C. Alix Timko
Reviewer #1:

The revisions to the manuscript address well the concerns raised regarding in the first draft. Your re-organization and editing of the Methods/Study Design and Background sections are excellent and greatly improve the flow of the paper. In particular, the way that you have explained the relationship between cognitive flexibility and perfectionism/compulsive behaviors on p. 5 does a good job in explaining the connection between the empirically supported neurocognitive weaknesses (set shifting and central coherence) and expression of those problems in a perfectionistic thinking style.

Thank you. We are happy that the reorganization improved the flow. We appreciate your recommendation.

Background:

1. The Objectives Section is a very helpful addition that clarifies the specific outcomes being measured (pp. 8-9). The last paragraph of the Rational for CRT section (top of p. 8) also describes the aims, but the way that they are set out is not very consistent with the Aims in the Objectives section, which comes next. For example, the pilot and feasibility RCT aims of "pilot recruitment, randomization procedures, and assessment batteries" in this paragraph at top of p. 8 are described as "recruitment, treatment administration, and participant retention" and "assessment battery" in Primary Aims below. A suggestion is to make these two sections more consistent.

Thank you for pointing this out. We wanted to avoid redundancy in the two places, so we chose to revise the statement at the end of the rationale section and provided more detail in the primary aims.

Methods/Study Design:

1. Description of Investigational Intervention: The clarifications about how you plan to standardize the intervention on p. 13-14 and in Table 1 make it much easier to understand how you plan to administer CRT. It seems overwhelming that you plan to administer all 11 of the CRT tasks listed for session 1 though, for example. I gather that you vary the number/types of tasks for each person based on personal performance?

We have added a clarification at the bottom of page 12 and top of 13 that not all tasks may be administered and that we will re-evaluate the tasks at the end of the study. Please know that some of these tasks take a few minutes. For example, the early stage illusions are often known to the adolescent (two faces or a vase?). The usually recognize it immediately and the discussion about
how they recognize it is very brief. Most tasks can be completed in one session. If an adolescent has more cognitive slowing due to malnutrition, then not all will.

2. Table 1. Typo in the Note - replace "CC-" with "CC="
Thank you for catching this. We have changed it.

3. Randomized Groups (pp. 13-14): The heading are currently "Teach the Parent (TTP)", "Contact Control - Family fun Time (FFT)" and "Treatment as Usual." I think you forgot to add the "CRT" aspect to each of the first two interventions - not all three randomization conditions receive CRT as described above. In other words: "CRT + TTP" and "CRT + FFT."

We added “cognitive Remediation Therapy” to the headings.

Also what is the minimum number of TTP and FFT sessions to be considered completion of the intervention? It looks like only 1 for TTP and 3-4 for FFT the way it is written.

We clarified that that 3 sessions of TTP or FFT would be needed on page 12.

4. Typo p. 15 line 17. "neuro-psychological" - this is spelled "neuropsychological" elsewhere
Corrected

5. Typo p. 16, line 9. "day of; discharge"
Corrected

Discussion

1. Suggestion to refer to the groups consistently throughout the manuscript, as CRT+TTP and CRT+FFT for example. Line four of Discussion references "CRT + contact control group" but it's CRT+FFT elsewhere.

We did this intentionally in the discussion as we wanted to highlight at the start of our discussion that FFT was designed as a contact control. We added (CRT+FFT) in parenthesis for consistency.
2. Aims/Outcomes - Suggestion again to keep these consistent throughout. In the Discussion you mention "not perceived as burdensome" to staff or families, but do not mention acceptability in your Primary Aims, even though you have outcome measures that do that.

We had not thought of this as being inconsistent as the issues of burden and acceptability are, our opinion part of determining the feasibility. Thank you for pointing out that this inherent assumption for us may not be made by others. We noted that we include these in feasibility in the primary aims.

3. Last sentence in paragraph on p. 21 does not need hyphen

Removed.

Reviewer #2: I believe the authors have adequately addressed my concerns and those of other reviewers. I appreciate changing the term "deficits" to "inefficiencies" as I agree this appropriately reflects what is found in the literature to date.

Thank you.

Editor: Thank you for addressing my comments. I have a few additional points to make:

1) Thank you for including an "Outcomes" section. Please could you now state the criteria (relating to each of the feasibility outcomes) that will be used to determine whether or not a future definitive trial will be carried out (eg recruitment rate > 50%, etc).

We have provided this information in the outcomes section.

2) Power analysis section (p32):

line 47: Add full stop after "feasibility".

line 51: Replace full stop with comma after "medium effect (f=.25)"

We completed the sentence after “feasibility” and added the comma.