Reviewer’s report

Title: Depression differed by midnight cortisol secretion, alexithymia and anxiety between diabetes types: a cross sectional comparison

Version: 1 Date: 14 Apr 2017

Reviewer: Emily Baron

Reviewer's report:

Thank you for giving me the opportunity to review this manuscript again, now entitled "Depression differed by midnight cortisol secretion, alexithymia and anxiety between diabetes types: a cross sectional comparison". I am happy to see that many of the reviewers' comments were taken into account and addressed. There are a few remaining minor comments that I have listed below. In general, the introduction and method sections are now more comprehensive, however the discussion is still a little thin, both in terms of findings' interpretation and implications. My major concern is that authors explain how different types of depression may have to be addressed differently in practice, but don't explain how this may differ among diabetes patients, or how detection/treatment may have to be tailored for this specific population.

Introduction:

- I see that authors have made an effort to describe different clinical features in more detail, but it is still unclear in places how these relate to depression, and more specifically, how these relate to melancholia and atypical depression. Eg. p5 line 96-100 and p5 line 103-107

- P5 line 108: perhaps worth explaining "Given the different aetiology of T2D and T1D, the aim was to compare the clinical features of the patients with T2D and T1D in terms of self-reported depression…etc."

Methods

- P7 line 134: please specify which aspects you are referring to

- Authors added 'data collection' as a subtitle in methods - perhaps best to use the term 'measures' and then separate this subsection into 3 sections and describe each measure under relevant section: 1) measures collected as part of the register and medical records; self-reported measures; 3) samples
- The authors added the section 'clinical psychiatric diagnoses' after the first round of reviews. Given that the authors now specify that they refer to self-reported measures when they discuss 'depression' or 'anxiety', I would suggest providing the classification numbers for melancholia and atypical depression when they first refer to them in the introduction. As for the clinical psychiatric diagnoses, the authors should be very clear that these were diagnoses made before recruitment, and collected as part of the medical records.

- P 7 line 151: The reason for collecting information relating to diabetes complications should be mentioned here (rather than in discussion p12 line 262-263)

- P 8 line 163-170 - I would take out the explanation of associations between the screening tools and antidepressants use etc. - this can be (and is) mentioned in the discussion, to help justify the use of screening tools rather than diagnoses. Plus, the evidence is not that convincing.

- How long before/after the self-report measures were the samples taken (MSC and HbA1c)?

- P 9 line 198: please explain what HbA1c is for the lay reader

- P 10 line (statistical analyses): explain analyses were conducted separately for both types of diabetes

Results:

- P 10 line 218-223: I think it's worth including the proportion of each sample who has a psychiatric diagnosis in table 1

- The authors refer several times to 'non-significant differences' - in instances when this refers to marginal p values, then rather say 'marginal difference' (e.g. p11, line 232 and 235); if there is no significant difference (p>0.1 for example), then don't say there is a difference at all - it's really misleading (e.g. p 12 line 268)

- The sections on p11 line 238-240, and line 246-248 should both go after the section describing baseline characteristics between T2D and T1D, and before you compare depressed vs non-depressed patients in both populations

- Page 11 line 241: to differentiate this section from the previous section (line 229-237), perhaps specify you are referring to adjusted associations.

- Authors explain in their feedback that they want to keep table 2 to be able to report prevalence etc. I understand that, but my suggestion was to drop the actual unadjusted non-parametric analysis from table 2. I suggest authors include the prevalence rates included in table 2, into table 3. This way only unadjusted and adjusted regression models are provided.
as statistics. Also, it seems a bit odd that some variables are included in table 3, but not in table 2. The analysis in the statistical analysis section of the methods would have to be adjusted accordingly.

- Why isn't BMI included in Table 3? Also in table 3, define acronym AOR in footnote, even if explain this in the text.

Discussion

- Section p12 line 253-255 - explain here whether these findings support or refute the hypotheses you outlined in the introduction

- The section on strengths and limitations should come after the interpretations of the findings, at the end of the discussion, before the conclusion.

- Similarly, the section on prevalence of depression p13 line 276-278 should come right after you report the prevalence in your study (p12 line 252); bear in mind that if the study you compare your results with did not use a screening tool, but rather used a diagnostic assessment, your results are not comparable.

- The section p13 line 280-252 should come right after p12 line 253-256

- When you report the use of screening tools as a limitation, the evidence you report as a rationale for the use of screening tools is quite weak - mere associations is not enough. You need to provide evidence of validation studies that have assessed the psychometric properties of the tools used in your study

- In the strength section of your discussion, p 12 line 258-260, you explain that the population was well defined. However, it was very restrictive, so your findings may actually not be representative of people with T2D and T1D in Sweden… this is worth mentioning.

- You also explain that both groups had the same average age, but that's because you explicitly excluded participants from the T1D who were less than 32 years old… so did you mean that you made sure the two populations matched by age so that age wouldn't bias the association between MSC and depression? If so, then state this.

- P 13 line 252-283: Authors state "We have not found any study where melancholia and atypical depression were compared between diabetes types." Rather state this earlier in the discussion, where you highlight the different association of depression among patients with different diabetes types, to emphasise the original findings of your research

- P14 line 300-309: authors explain how different subtypes of depression may be treated - but don't specify for which types of patients (T2D or T1D) this may be useful for. It seems you
discuss issues about subtypes of depression, but don't refer to how these may apply for patients with different types of diabetes

- I also feel that authors should report on the clinical differences found between the two types of diabetes patients, other than depression - were any differences or lack of differences found expected? Were any findings surprising etc?

Conclusion

- P14: line 311-314: state if the two types of diabetes indeed presented with what seemed like different types of depression, and state which (melancholia or atypical depression, or only partial presentation etc.). Nowhere in your paper do you actually say whether your hypothesis was supported or not.

- P14 line 315-318: sentence starting "To our knowledge…." This should go in the discussion section, before you explain how depression may be addressed

- P14 line 313 "The obesity prevalence was high in depressed T2D patients and low in depressed T1D patients" you repeat this several times in your article - please explain what this means and the implications this has in your discussion section

Grammar and typos:

Abstract:

- P 2, line 26-28: I appreciate that you've modified the aim, which is now a lot clearer, but perhaps rephrase to "The aim was to compare the clinical presentation of T1D and T2D patients in relation to self-reported depression, self-reported anxiety, alexithymia …etc."

- P2 line 47: This sentence is not grammatically correct; rephrase to "…was 80% for T2D depressed patients and 6% for T1D depressed patients"

Introduction:

- P6 line 115-116: Rather "Being able to differentiate between melancholia and atypical depression can (not might!) have clinical implications…"
Method:
- P 9 line 195-196: this sentence is not grammatically correct. You could rewrite this is this way "The number of T2D and T1D patients recruited were 9 & 60 in spring, 5 and 34 in summer, and 10 & 54 in autumn/early winter, respectively.

Results:
- p10 line 217: TID (with a capital i), rather than T1D

Discussion:
- p 12 line 253-255: rather begin the sentence with 'In T1D patients', rather than say this at the end
- p 12 line 271: start a new paragraph with "Another limitation is that depression and anxiety…"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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