Reviewer’s report

Title: The role of oxytocin receptor gene (OXTR) DNA methylation (DNAm) in human social and emotional behaviour: a systematic narrative review.

Version: 0 Date: 04 Jan 2018

Reviewer: Alessandro Serretti

Reviewer's report:

The present manuscript aims to review the role of oxytocin receptor gene (OXTR) DNA methylation (DNAm) in human social and emotional behavior. Although this issue is a worthy topic of investigation because of the effect of OXTR DNAm on human behaviors are far to be elucidated, the present review fails to provide both a global picture of the field and possible future directions for research on this issue. Indeed, the review provided a summary of the previous studies on this issue, failing to integrate the different results in a unified view. Taking into account that reviewed studies are greatly heterogeneous both in methods employed and population investigated (and a large number of them were underpowered for epigenetic and genetic studies), Authors should better discuss the differences in their methodology, ideally providing suggestions to improve the further research in this field. More in detail, the manuscript should be revised accordingly to the following suggestions.

Abstract

A brief background about the effects of OXT in human social and emotional development should be provided also here.

It is not clear what Authors mean with "a range of mental health outcomes". Please, clarify. Furthermore, the broad focus of the review on "a range of mental health outcomes" represents a limitation of the paper, because of the inclusion of very different populations (e.g. healthy subjects and Autism Spectrum Disorder subjects). Although I understand that studies on OXTR DNAm are still few and Authors had to include different population in their review, they should better stress the possible differences on OXTR DNAm due to the diagnosis.

Taking into account the little number of studies included and the broad differences among them, Authors should be more cautious in their results and conclusions.
Background

Actually, the research on the effects of OXT on human social and emotional behaviors started far before than five years ago. Please, correct.

A brief background about the social and emotional effects of OXT intranasal administration should be added.

Method

Authors should better specify what they mean with "social and/or emotional outcome" because from table 1 it seems that they considered as outcomes diagnosis, psychometric scales, neuroimaging findings, and so on. Further, Authors stated that they included articles investigating "epigenetic regulation of OXTR and its association with social or emotional behaviors in humans, including [...] mood problems (depression and stress), behavioral problems (eating disorder and callousness) and rarer neurodevelopment disorders (autism)", raising again the question about how the outcomes were selected (e.g. eating disorder are far different from "callousness", as well as major depressive disorder from stress). Please, clarify and better stress these issues as limitations of the present review.

Results

Authors should refer to table 1 for detail, avoiding to report detailed information in the text about the different studies included in the review.

Narrative synthesis of emergent findings

Overall, this section seems to provide only a brief summary of previous studies, failing to critically discuss the different findings and to give to the reader a global picture of the field.

Although the studies on this issue are still few and consequently it is difficult to make a review on this issue, Authors may provide suggestions on methodology to improve the quality of future studies as well as they may include a section on findings in animal models.

Furthermore, Authors cited genetic findings together with epigenetic ones, making the text quite difficult to follow. Maybe, Authors should dedicate a section to genetic findings, better stressing the relationships among genetic variants and the epigenetic status.

As stated above, the inclusion of very different populations may limit the comparability of the different findings. This issue should be better stressed and discussed by Authors.
Conclusions

Authors should revise the conclusions according to the previous comments.

Taking into account the several limitations of the studies included, Authors should expand the paragraph about the future directions of research in this field, providing useful suggestions to improve the quality of future studies.

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

No

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

Unable to assess

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

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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None

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