Reviewer’s report

Title: Association of brain-derived neurotrophic factor levels and depressive symptoms in young adults with acne vulgaris

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Reviewer: Marc L. Molendijk

Reviewer's report:

The authors investigated serum BDNF levels in persons with acne vulgaris (depressed and non-depressed) and healthy controls. They find particular low BDNF levels in depressed patients with acne.

This may be an interesting study, in my view especially when the points below are thoroughly addressed.

- The mean values of BDFN levels and the ranges (I assume it are ranges, because this is not specified) are exactly the same (two decimals) in depressed patients and controls. This is possible, but very coincidental. It may be a typo. It doesn't hurt to check once more.
- Mention in the abstract that cross-sectional data is used
- Talk about depressive-symptoms, and not depression (throughout the manuscript).
- The conclusion in the abstract can be written in a single sentence I think
- It does not make sense to use BDNF as a screen in terms of risk for depression. The model that the authors present is overfitted and only applies to this data (you need cross-validation; predicting associatons as they are in te data does not make sense).
- I think it is better to speak in terms of 'patients / persons with depression' instead of 'depression patients').
- When referring to the mechanisms, please refer to shortcomings of the preclinical research in this field (in introduction and discussion), notably the lack of validity of the animal models used, eg:

Coping with the forced swim stressor: towards understanding an adaptive mechanism
Neural Plasticity, 2016 - hindawi.com

In the forced swim test (FST) rodents progressively show increased episodes of immobility if immersed in a beaker with water from where escape is not possible. In this test, a compound qualifies as a potential antidepressant if it prevents or delays the transition to this passive

Immobility in the forced swim test is adaptive and does not reflect depression

Psychoneuroendocrinology, 2015 - Elsevier

The forced swim test is based on the progressive immobility a rodent displays when immersed in a beaker filled with water from where no escape is possible. While the test was originally designed to identify the antidepressant potential of drugs, over the past decade a …

- When presenting meta-analytic evidence that depression is associated with low BDNF, do not use the outdated meta-analysis by Sen (ref 15) but an updated one, eg:

Serum BDNF concentrations as peripheral manifestations of depression: evidence from a systematic review and meta-analyses on 179 associations (N=9484)

Molecular Psychiatry 2014 - nature.com

Abstract Meta-analyses, published in 2008-2010, have confirmed abnormally low serum brain-derived neurotrophic factor (BDNF) concentrations in depressed patients and normalization of this by antidepressant treatment. These findings are believed to reflect

- Also, and related, discuss the lack of associations between BDNF and depression (severity) from the largest -longitudinal - cohort on this subject (in introduction and discussion):

Serum levels of brain-derived neurotrophic factor in major depressive disorder: state-trait issues, clinical features and pharmacological treatment

Molecular …, 2011 - nature.com
Recent evidence supports the neurotrophin hypothesis of depression in its prediction that brain-derived neurotrophic factor (BDNF) is involved in depression. However, some key questions remain unanswered, including whether abnormalities in BDNF persist beyond the …

Chronic depression is associated with a pronounced decrease in serum brain-derived neurotrophic factor over time

Molecular Psychiatry, 2015 - nature.com

One of the leading neurobiological hypotheses on depression states that decreased expression of brain-derived neurotrophic factor (BDNF) contributes to depression. This is supported by consistent findings of low serum BDNF levels in depressed patients compared …

- With regard to confounders use and refer the following reference. In the reference, the importance of storage time and temperature on BDNF is also shown. How was BDNF stored in your study and at which temperature. Were there differences between patients and controls?

Determinants of serum brain-derived neurotrophic factor

Psychoneuroendocrinology - ..., 2011 - Elsevier

Background Brain-derived neurotrophic factor (BDNF) belongs to the neurotrophin family of growth factors and affects the survival and plasticity of neurons in the adult central nervous system. The high correlation between cortical and serum BDNF levels has led to many …

Geciteerd door 195 Verwante artikelen Alle 12 versies

- Also, and related, there are strong seasonal effects in BDNF, read the following paper and show that seasonality did not affect your results.

Serum BDNF concentrations show strong seasonal variation and correlations with the amount of ambient sunlight
Earlier findings show seasonality in processes and behaviors such as brain plasticity and depression that in part are regulated by Brain-Derived Neurotrophic Factor (BDNF). Based on this we investigated seasonal variation in serum BDNF concentrations in 2,851 persons.

- The table titles sound really weird to me
- Some English editing is need (eg. the sentence in the discussion stating that 'Neurotrophic factor hypothesis is stating that …'
- The conclusion in the discussion sounds weird. The final sentence of the manuscript is disturbingly vague. The sentence on line 20 on this final page should be deleted: BDNF is not a strong marker for … as stated above).

**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.
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.
I am able to assess the statistics

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