Author’s response to reviews

Title: Associations between (sub)clinical stress- and anxiety symptoms in mentally healthy individuals and in major depression: A cross-sectional clinical study

Authors:

Georgia Konstantopoulou (geokonstantop@gmail.com)
Theodoros Iliou (theo_taison1@yahoo.gr)
Katerina Karaivazoglou (karaivaz@hotmail.com)
Gregoris Iconomou (giconomou@gmail.com)
Konstantinos Assimakopoulos (kassima@upatras.gr)
Panagiotis Alexopoulos (panos.alexopoulos@upatras.gr)

Version: 3 Date: 15 Jul 2020

Author’s response to reviews:

Dear Editor,

We would like to thank you for your message and the 3rd reviewer’s comments. In the following lines you can find our point-to-point responses and the changes we have made to our manuscript in response to the reviewer’s comments. We hope that you will consider the revised version of our manuscript worth publishing it in BMC psychiatry.

Yours sincerely
P. Alexopoulos

Reviewer reports:
"In this study, the authors assessed possible associations between stress and anxiety symptoms, patients with major depression and mentally healthy individuals of different age clusters and occupations. They found that stress levels were related to clinical anxiety while neither group identity nor age exerted any influence on anxiety levels. The study pointed out the putative relevance of mild stress as a target for early interventions to prevent the onset of anxiety disorders. The study is well designed and the manuscript well written. It's a cross-sectional study that enrolled students and employees from the University Of Patras as controls as well patients suffering from depression. In the methods section, the authors should clarify inclusion and exclusion criteria for healthy subjects as well the selection procedure for this study. Please see bellow, the relevance of this for discussion."
Response: We have modified this part of the methods section and the inclusion and exclusion criteria for both controls and patients with major depression, as well as the selection procedure are now clearly depicted.

From the manuscript:
The current cross-sectional investigation included (1) a group of patients with major depression and a convenience sample of mental healthy individuals consisting of (2) undergraduate students, (3) postgraduate students and (4) employees of the University of Patras. The inclusion criteria for patients with major depression were willingness to participate in the study after detailed presentation of the study aims and procedures and a current episode of major depression. The exclusion criteria included the presence of a mental disorder other than major depression and/or incapacity to give written informed consent. The inclusion criteria for mentally healthy individuals were willingness to participate in the study and absence of a current episode of a mental disorder being treated with pharmaco- and/or psychotherapy. The exclusion criteria included being on psychotherapy and/or on medical treatment because of previous episodes of a mental disorder and/or incapacity to give written informed consent. The study was conducted between April 2018 and October 2019. Patients suffering from major depression fulfilled the DSM 5 criteria for major depression and were recruited at the afternoon outpatient clinic of the Department of Psychiatry of the Patras University General Hospital and at the Special Health Service Unit of the University of Patras, Greece. The diagnosis of major depression was established by an experienced psychiatrist who had examined the patient and had coordinated the diagnostic workup (e.g. brain imaging, neurocognitive assessment). The mentally healthy undergraduate students were students of the School of Humanities and Social Sciences of the University of Patras and were recruited at seminars and other didactic activities. Postgraduate students were recruited at the one-day health, safety and security seminars for first-year postgraduate students of the University of Patras. University employees were recruited through word-of-mouth. The study was approved by the Bioethics and Research Ethics Committee of the University of Patras. All procedures performed in the study were in accordance with the 1964 Helsinki declaration and its later amendments.

The results are presented in a correct way. The discussion addresses and discusses the results of the study as well its main limitations.
My main concern relates with control group characterization, inclusion and exclusion criteria as well the absence of depression evaluation in the control group. I think that this issue should be clarified and added to the limitations of the work. The absence of a measure of depressive symptoms in the control group reduces the generalizability of the results. How did the authors ensure there weren't depressive patients among the control group?

Response: we have added this point to the list of study limitations. Since we have not employed a depression scale, we cannot exclude the presence of subclinical or very mild depressive or anxiety symptoms in controls. Nonetheless, the presence of a clinical mental disorder and/or being on medication or psychotherapy was an exclusion criterion for the participation of individuals without major depression in the study.

From the manuscript:
…Fourth, unfortunately depressive symptoms were not captured with a depression scale (e.g. Hamilton Depression Rating Scale or the Beck Depression Inventory) either in patients who
suffered from major depression or in mentally healthy individuals. Despite the high diagnostic validity of modern diagnostic criteria for major depression[23], the presence of subclinical or very mild depressive symptoms, not justifying the diagnosis of a clinical depressive or anxiety disorder, cannot be precluded.

I think that it should be improved by discussing adding a paragraph about the potential overlap between depression and anxiety. Other studies in university students (Vanessa Silva et al, 2017) have found that high anxiety trait is a predisposing factor for persistent high depression levels. As mentioned before, this overlap could have influenced the results of the present study since depression levels were not assessed in the study.

Response: This issue is now thoroughly discussed in the limitations section of the manuscript.

From the manuscript:

Fourth, unfortunately depressive symptoms were not captured with a depression scale (e.g. Hamilton Depression Rating Scale or the Beck Depression Inventory) either in patients who suffered from major depression or in mentally healthy individuals. Despite the high diagnostic validity of modern diagnostic criteria for major depression[23], the presence of subclinical or very mild depressive symptoms, not justifying the diagnosis of a clinical depressive or anxiety disorder, cannot be precluded. Recently, high proneness of medical students with high levels of trait anxiety to clinical depression and particularly to persistence of depressive symptoms was reported [48]. Even though, the levels of trait anxiety in the groups of the present study were relatively high [28], it is underscored that the presence of a clinical depressive or other mental disorder was an exclusion criterion for recruiting mentally healthy individuals.