Author's response to reviews

Title: Lack of cortisol response in patients with PTSD undergoing a diagnostic interview

Authors:

Iris-Tatjana Kolassa (Iris.Kolassa@uni-konstanz.de)
Cindy Eckart (Cindy.Eckart@uni-konstanz.de)
Martina Ruf (Martina.Ruf@uni-konstanz.de)
Frank Neuner (Frank.Neuner@uni-konstanz.de)
Dominique J.-F. de Quervain (Quervain@bli.unizh.ch)
Thomas Elbert (Thomas.Elbert@uni-konstanz.de)

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Author's response to reviews: see over
Dear Editor,

Thank you very much for your response to our manuscript 1208488813659834 „Lack of cortisol response in patients with PTSD undergoing a diagnostic interview“ and the opportunity to address the reviewers comments. Below, we indicate how we have changed the manuscript in response to the reviewers’ suggestions:

Reviewer 1:

Point 1: Regarding the results, I was not surprised to see this non-responses on the basis of the literature (that is also cited by the authors). On the other hand, the trauma victims might have shown a small cortisol response to the "stressful" interview, but the response peaks may have been missed by the timing of saliva collection (intervals between samples were about an hour). So I am left with the question, what is the main message for the reader of this paper?

Response: The main message is that PTSD patients in the supposed stress condition showed a nearly identical course of cortisol levels as those in the control group. Correspondingly, ratings of subjective well-being showed no evidence of higher arousal and unpleasantness ratings in the stress group compared to the control group. Thus, addressing traumatic experiences within a safe and empathic environment appears to impose no unacceptable additional load on the patient. However, we emphasize that such a diagnostic interview imposes high demands on the interviewer, who has to be supportive, empathic, create a secure environment and give the client maximal control over the situation. This has been clarified both in the abstract and in the conclusion of the manuscript.

Reviewer 2:

Major Compulsory Revisions:

Point 1a: The whole idea of the study is around cortisol and psychological response to a stressor, i.e. the interview regarding the traumatic experiences. However, virtually no information is given with regard to this interview apart from the fact that it is “detailed and standardized”. The reference given refers to an unpublished manuscript in German. The authors need to present this interview in detail, especially...
given that their findings regarding lack of psychological response are very surprising.

**Response:** Both the English and the German version of the questionnaire can be downloaded from the vivo foundation website ([www.vivo.org](http://www.vivo.org)) under the vivo publication link. This information has been included in the manuscript.


**Example items of the questionnaire are:**

1. Were you beaten? If yes, on which body parts (head, body, feet, genitals)?
2. Were you blindfolded?
3. Did you receive electric shocks?
4. Did you witness how other people (relatives, friends, strangers) were tortured?
5. Were you forced to maltreat or torture fellow prisoners or relatives?
6. Were you forced to take off all your clothes? In which situations?
7. Were you isolated from other people and fellow prisoners? For how long?
8. Were you systematically prevented from sleeping?
9. Were your genitals touched against your will?
10. Were your genitals twisted or squeezed?
11. Were you forced to sexual intercourse or were objects inserted in your anus or genitals? If yes, how many people were involved?
12. Did you experience mock executions?

**Point 1b:** Generally, trauma- and trigger-associated arousal and distress is a hallmark of PTSD. Accordingly, the most established psychological treatment of PTSD (exposure therapy) is based on initial arousal and consequent habituation and memory consolidation over time. Therefore, the authors not only need to present the interview in greater detail but should also discuss why their findings might differ from what is commonly seen in patients with PTSD.

**Response:** We agree that high arousal and distress in response to trauma reminders are very common in PTSD. However, participants were already very aroused and distressed when we started the interview, which is consistent with our experience within our Psychotrauma Research- and Outpatient Clinic for Refugees. We argue that this may have induced a ceiling effect.

However, the main thrust of the manuscript is the lack of a cortisol response to trauma reminders, and in that area there are very few comparable studies. We have added the case study of Otte et al. (2002) to the study of Elzinga et al. This case study, in which a PTSD patient underwent imaginal exposure therapy, is most directly comparable to the present experimental procedure, where subjective distress was very high during the first session and much lower during the 20th session – while there was no accompanying cortisol response, and cortisol dynamics were
essentially the same during the first and the 20th session. We have included the study by Otte et al. in the introduction and discussion sections.

**Point 2:** According to the methods section, all of the 33 participants were suicidal (9 of them with severe suicidality), which is very unusual and poses many ethical challenges in a research context. First, the authors should double-check if really all participants were suicidal (how was suicidality assessed?) and if so, how did the authors ensure referral to psychiatric treatment, hospitalization, etc.?

**Response:** Suicidality was assessed by Part C of the German version (Ackenheil et al., 1999) of the M.I.N.I. Mini International Neuropsychiatric Interview (Sheehan et al., 1997, 1998). This has been stated more explicitly in the manuscript. Double-checking did not change reported suicidality.

The high level of suicidality is common for the population we examined. In our Psychotrauma Research- and Outpatient Clinic for Refugees we treat traumatized refugees with mostly severe forms of PTSD. Those people generally have lived in Germany for 2-5 years in refugee shelters, where living conditions are poor. Most refugees are not allowed to work, they have no distraction from their mental problems and live surrounded by people with similar traumatizations. These people feel guilty because they cannot provide better living conditions for their children and they feel extremely helpless because of their insecure state of asylum and the constant threat of deportation to their home countries. Besides the mental strain of the traumatic experiences, the bad living conditions for refugees in Germany are one reason why these people are so severely suicidal. The other reason is that they would prefer to die before going back to the country where they experienced the severely traumatic experiences (a form of PTSD avoidance behavior).

We assess for immanent risk of suicide, and patients with well-formed plans for times or location of suicide are hospitalized. However, we refrain from referring those people to psychiatric clinics as long as clients convincingly accept no-suicide contracts. Compulsory referral to a clinic can be harmful for the patient because he again loses control over his situation and is rendered helpless – a situation these people have experienced already far too often. In addition, patients would be even further removed from their compatriots at a clinic, where no one would even speak their language.

We assure reviewer 2 that we do our best to ensure the safety of our clients and to improve their mental health and living conditions. Members of our lab write numerous reports for court purposes and testify in court as to whether specific refugees truly fulfill criteria of PTSD and what the causes of their PTSD symptoms appear to be. However, the worst thing that could happen, and that sadly does happen, is that asylum lawsuits end negatively and people are suddenly deported, sometimes even out of psychiatric hospitals.

**Minor Essential Revisions:**

**Point 1:** Regarding table 1, no subscales of the PDS are needed. What is needed is the distribution of the medication, BMI, Age, smoking, etc. between groups and in case there are between-group differences covarying for these variables in the analyses.

**Response:** We would prefer to keep the PDS-subsubscales because one could have the hypothesis that hyperarousal symptoms are particularly related to cortisol levels.
There was no significant difference between groups regarding age: $t(31)= -0.82, p =.42 \ (M_{Controls} = 33, SD = 7.9; M_{stress\ group} = 35, SD = 7.4)$. Eight individuals from the control group and 8 individuals from the stress group were smokers. Corresponding information has been included in the manuscript.

Information on medication: 9 participants took antidepressants (stress group: 4, control group: 5), 6 took neuroleptics (stress group: 3, control group: 3). Limiting the analysis to individuals without medication did not change the pattern of results. Furthermore, taking medication into account also did not change results. This information was also described in more detail in the manuscript.

Participant’s BMI is not available. However, because of the limited food packages refugees are provided by public authorities, participants are in a rather homogenous normal weight range, with no one being obese or anorectic.

**Point 2:** According to table 1, patients slept on average 3.2 hours the night before the examination indicating severe hyperarousal. Even for PTSD patients this can be considered and it seems all the more surprising that the interview did not elicit a psychological response. The authors should comment on this.

**Response:** As indicated above, the patients we investigated are severely traumatized and present severe PTSD symptoms. Among the patients of our Psychotrauma Research and Outpatient Clinic for Refugees, we frequently observe only 3 hours of sleep, interrupted by nightmares and lying awake in the bed without being able to sleep. We agree that it is surprising that these people do not respond at least psychologically to trauma reminders. We think that a ceiling effect might be the reason, which has now also been indicated in the manuscript.

**Point 3:** In the results, it is stated that the “participants performed extremely poorly”. However, no control group is mentioned. Are there established cut-off values, etc. with which the performance of the participants could be compared.

**Response:** There are no established cut-off values. However, we recruited 16 healthy subjects (9 male, 7 female; mean age 30 years) and tested their performance in the DMS task. These controls made errors in 1.5% of trials compared more than 30% errors in the PTSD sample. This information has been included in the manuscript.

Discretionary Revisions:

**Point 1:** I think the introduction is much too long. For example, the information regarding AVP or pharmacological challenge is not needed to my mind.

**Response:** We have found that the stress response and especially its endocrine cascade is often presented in a very abbreviated form in the literature and would prefer to give a more detailed account here. We also believe that as we study a non-pharmacological challenge, giving some information on what is known about pharmacological challenges is appropriate.

**Point 2:** Could the fact that every interview was done with the help of a translator at least in part explain the lack of response?

**Response:** The translators are trained to translate exactly what the interviewer said. The questions reminded the participants of their traumatic experiences and they showed
appropriate behavior (tension, tears in the eyes etc.) upon translation. Besides that the interview takes somewhat longer because of the additional time for translations. We do not see how this factor should affect cortisol responses.

**Point 3:** Figure 3 is not needed

*Response:* We have removed Figure 3.

We hope that we have properly addressed the critical points raised and that the manuscript is now more suitable for publication in *BMC Psychiatry*.

Sincerely yours,

Iris-Tatjana Kolassa