Author's response to reviews

Title: Gender differences in patients with dizziness and unsteadiness regarding self-perceived disability, emotional distress, symptom severity and its associations

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Author's response to reviews:

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Point-by-point description of the changes made.

First of all we would like to thank the reviewers for their work, time and the valuable points of critique.

Title: Gender differences in patients with dizziness and unsteadiness regarding self-perceived disability, emotional distress, symptom severity and its associations

New title: Gender differences in patients with dizziness and unsteadiness regarding self-perceived disability, anxiety, depression, and its associations.

We adapted the title with respect to the corrected primary aim of the survey.

Reviewer: Christoph Best

Comment (1) Abstract:
The abstract is concise and delineates the main points of the study. However, we would recommend the write “the genders do not significantly…” instead of “sexes” (Minor Essential Revisions).

Response: We exchanged the word “sex” by “gender” in the whole manuscript.

Comment (2) Introduction:
We would suggest re-organizing the introduction more clearly:

Within the first part of the introduction descriptions of the rates of prevalence of vertigo and dizziness as well as prevalence numbers for coexisting anxiety and depression as well as further psychological distress factors should be given in
Within the second part background on gender differences with respect to psychological strain as anxiety and depression should be given.

This will then automatically lead to the main questions raised by the authors. As it is at the moment, the authors start with general prevalence on vertigo and dizziness, switch to a differentiation of the HADS between the genders, go back to general information on anxiety and depressive prevalence in vertigo and dizziness patients and then go back again to gender differences. This should clearly be separated, it will read much easier and the succeeding main questions of the study will then be presented as logical results of the objectives. With respect to the reader, this will improve the introduction (Minor Essential Revisions).

Response to the reviewer

We re-organized the introduction with respect to your suggestions.

Comment (3) Introduction:

At the end of the introduction, the authors state their main objectives:


(2) Whether female/male differ in the prevalence of severe disability, anxiety and depression.

(3) Whether female/male differ in the associations of these aspects.

What exactly is the difference between objective (1) and (2)?

Do the authors differentiate between self-perceived disability… and prevalence of disability? And if the authors do differentiate between these two, what is the reason?

We would suggest, to reduce the main objectives to differences between the genders with respect to disability, anxiety and depression as main objective. This should than be stated as primary end-point. In a second step, the differences between the associations of the above mentioned aspects should be added as secondary and pure descriptive end-point. If the authors will not change the main objectives (1) – (3) please explain why! (Major Compulsory Revisions)

Response:

We differentiated between 2 ways of measuring self-perceived disability, anxiety, and depression: We calculated 1.) the median values of the questionnaire scores (DHI, VSS, HADS-A, HADS-D) to describe “the level” of self-perceived disability, symptom severity, anxiety and depression, and 2.) frequencies, in order to estimate the prevalence rates of self-rated severe disability, abnormal anxiety and abnormal depression. For the second analyses we defined dichotomous variables.

We adapted the objectives according to your suggestions (p 5/6)
Comment (4) Methods:
In the description of the inclusion criteria the authors state, that the problems had to be “associated with a vestibular disorder”. What does that mean? And what does “problems” mean? Does this mean that the symptoms and complaints of the patients had to be caused by a vestibular disorder? If so, please change the writing of the inclusion criteria. The term “problems had to be associated with vestibular disorders” is in no way scientific and does not reflect a distinctive diagnostic procedure! (Major Compulsory Revisions)

Response: We rewrote this section (p 6).

Comment (5) Methods:
In the exclusion criteria section, the authors mention psychic disorders as exclusion criteria. How were psychic disorders diagnosed? On the basis of the clinical impression? On ICD-10 criteria? By SCID interview? This needs to be defined much more clearly, especially, as the authors analyse data from patients with high rates of anxiety and depression. The likelihood of co-existing manifest psychiatric disorder therefore is extremely high and the diagnostic procedures have to be described more in detail! (Major Compulsory Revisions)

Response: We rewrote this section (p 6/7).

Because in patients included in the survey the diagnosis of a vestibular disorder was made in the context of a previous or the present neuro-otological workup, and the begin of the patient’s symptoms and complaints was associated with the time of the vestibular diagnosis, we assume that patients with primarily psychiatric causes of vertigo, dizziness and unsteadiness were excluded. Patients were not assessed routinely by psychiatrists, but by neurologists.

Comment (6) Methods:
In the section of the statistical analyses it is not described, if a correction for multiple testing was performed. If such a correction was not performed, it has to be stated, that all results are descriptive purely, and significance levels do not reflect results with respect to a hypothesis controlled calculation, but are presented to describe possible effects! (Major Compulsory Revisions)

It is not mentioned, if the main objectives were planed as end-point hypothesis or if the overall analysis of the data was planed as a descriptive analysis. This information is mandatory! (Major Compulsory Revisions)

Response
You are right that we did not adjust the significance values with respect to multiple comparisons. For the revision we corrected the statistics and adjusted the significance values (p 9/10; Tables 2, 3, and 4). In each case our results are descriptive purely.

Comment (7) Results:
(7.1) The major flaw within the presentation is the character of analyses. On table 1 seven statistical tests have been performed. The strongest effect is described with a p-value of 0.018. Applying a Bonferroni adjustment to these results, not a single significant p-value will remain. Therefore, it is absolutely mandatory to mention, if the adjustment for multiple testing was done or if the results are presented as descriptive analysis.

Response:
We corrected our statistics as mentioned above. We adapted the tables to make the results of the different investigations (primary objective: gender difference in the mean level of self-perceived disability, anxiety and depression; gender differences in the prevalence of self-rated severe disability and abnormal anxiety and depression; secondary objective: gender differences in the associations between disability, anxiety and depression) better readable.

Comment (7.2)
Furthermore, the diagnostic classification of the patients is not detailed. The authors only differentiate between unilateral peripheral, bilateral peripheral, central vestibular and multifactorial disorders. The present 36.1% of central vestibular disorders, which is in contrast to 13.2% of central vestibular disorders in a large analysis from Strupp and co-workers (Strupp et al., 2003). In this analysis, only 3.6% of the patients showed bilateral vestibular pathology, while the authors present 8.4%. Therefore, the distribution to the diagnostical subgroups is contradicting previously data. We therefore recommend, to show a detailed diagnostical classification. (Major Compulsory Revisions)

Response
Because the data analysed in this survey were primarily collected to investigate the reliability and validity of the German version of the Dizziness Handicap Inventory, we are limited in giving more detailed information. Two of the authors, both physiotherapists, screened the clinical reports of the included patients to find the diagnoses and co-morbidities. In the case of uncertainty or missing information they contacted the physicians.

For this revision we repeated the investigation of our records and adapted the groups of diagnoses (Table 1) by adding ‘psychophysic dizziness', vestibular migraine and ‘multiple vestibular disorders'. We furthermore report in a new additional table 1 the distribution of female and male patients in some more specific diagnoses.

You mention that our distribution of different vestibular pathologies differs from the one described by Strupp at al. 2003. Previous surveys differ considerably in the composition of the study population, not only with respect to the diagnoses. Therefore the characteristics of the study-population have to be taken into account when interpreting the study results. We added this aspect in the discussion part: p 15/16.
Comment (7.3)
On table 2 we count 74 statistical significant tests. Again, a clarification is needed, was this adjusted for multiple testing, or are the results descriptive. (Major Compulsory Revisions)

Response: Please look at our response to comment 6 and 7.1.

Comment (8) Results:
(8.1) On table 3 and 4 data from 200 patients is presented. The authors included 202 patients in their analyses. Where are the 2 missing male patients? (Major Compulsory Revisions)

Response:
You are right. In 2 cases we controlled the completeness of the patient questionnaires to late and were not able to contact these men to fulfil the HADS. We added this point in the result section: p 10.

Comment (8.2)
In addition, table 4 needs some design work over. Especially the categories anxiety and depression on the lower section are confusing, it presented that way. (Minor Essential Revisions)

Response: The most important information of the previous submitted table 4 is now reported in table 3. We decided to restrict our results regarding the prevalence of abnormal anxiety and depression to the results based on the cut-off criteria of the German version of the HADS. We hope this makes the results and the table easier to understand.

Reviewer: KATHRINE JAUREGUI-RENAUD

Comment (9) Background
Since the study was designed to assess gender differences and to compare the results with the general population, the introduction should give the reader a better background about studies looking at the relationship between gender and mental disorders, particularly anxiety and depression (including changes through time and space); as well as previous findings from international studies and studies made within the same socio-economic/ cultural context (eg. Switzerland), on the prevalence of anxiety and depression in both, patients seeking medical care and the general population.

Response:
As you saw it in the list of references we discussed whether we should give more general information about prevalence rates of anxiety and depressive disorders as well as gender specific differences in general populations. We decided not to do it because relevant surveys report a broad spectrum of different values and this information might distract from our main questions. For the reader who is
interested in more detailed knowledge about prevalence rates of anxiety and depression we listed relevant references in the discussion section. In the introduction we explain why we chose the reference values estimated by Hinz and Schwarz. They are based on the HADS, which we also applied. Furthermore the survey was performed in Germany, which lies close to Switzerland and might be comparable regarding the most important socio-economic and cultural characteristics.

A comparison of our prevalence rates with other patients seeking for medical help would be interesting but we would like to focus on information which is relevant for professions assessing and treating patients with dizziness, vertigo or unsteadiness.

We considered your input about the effect of time in the onset respectively development of depression. Wittchen et al. (2000) in Germany and Merikangas et al. (2003) in Switzerland supported in prospective-longitudinal community studies that individuals with anxiety states alone tended to develop either depression or co-morbid anxiety and depression. This could be an explanation why in our sample in both genders the prevalence rates of anxiety and depression are of nearly the same size (p 14).

Comment (10) The rationale behind the choice (or not) of potential confounding variables is not reported (eg. socio-demographic characteristics like employment status, marital status and level of education; comorbidities as well as potential stressors).

Response

Like mentioned above the data for this study were primarily collected to investigate the reliability and validity of the German version of the DHI [24,26]. In the submitted manuscript we did not report all of the collected information. In the revised manuscript and tables we added information about the patients living conditions, employment status (Table 1) and need of personal assistance (in the section results). We re-assessed our records and report newly co-morbidities in the new additional table 2. But the number of specific potential confounding variables is not complete. We added this limitation in the discussion section (p 15/16).

Comment (11) Methods

(11.1) There is no explanation about how the study size was calculated, both to compare groups and to estimate prevalence.

According to the main objectives, there is no explanation to support why the sample sizes are so unequal, when the main outcome would require a design to optimize comparisons between two groups (while considering interactions).

Response:

We calculated the study size for the exploratory factor analysis of the DHI-G but not for this survey. You are right that this is a relevant flaw of our survey. Furthermore it is true that for the investigation of the main objectives of this
survey an equal number of female and male patients would have been adequate. We added these points as limitations (p 16).

I would like to mention that the proportion of female and male patients in our study population is comparable with the ones of other populations [Piker et al. 2008; Grunfeld et al 2003; Monzani et al 2001; Mendel et al. 2001; Yardley et al. 1998].

(11.2) There is no description of: the sampling technique, the number of eligible subjects, the subjects examined for eligibility and those who were excluded for the analysis (eg. missing data).
Also there is no report on the number of subjects declining to participate.
Response:
The recruitment was done consecutively. We added this information in the section procedure (p 6).
Based on our records we retrospectively investigated the percentages of female and male patients who entered the center during the time of recruitment, who answered our letter of enquiry, who were willing to participate, and the percentages of both genders who were included and excluded in the survey (p 10 and/or Figure 1).
In the revised manuscript we report the missing data of two subjects (p 10).

Comment (12)
(12.1) The description of the characteristics of the participants is not including their general socio-demographic characteristics, at least: the employment status, the marital status and the level of education.
(12.2) The age interval and the age distribution of the 2 groups are not described.
(12.3) The description of the vestibular disease is not complete; the information about recurrent vertigo and more specific diagnostics are missing. The diagnostic criteria should also be described.
There is no information about co-morbidities.
Response:
(12.1) We added in table 1 information regarding the living condition (alone, with partner, with partner and children, with children) and employment status.
(12.2) In table 1 we reported the mean (SD) age in female and male patients. We completed the inclusion criteria in the section ‘method’. We restricted the recruitment to patients aged 18 to 75 years (p 6).
(12.3) Please read our response to comment (7.2). We retrospectively assessed our records and gave a list of co-morbidities (dysfunctions in selected body structures) in the new additional table 2.

Comment (13) The manuscript describes a bivariate analysis, including multiple comparisons and correlations (apparently without significance corrections), which
may be exploratory. However, the results of a multivariate confirmation of the findings (including potential confounders) are not described.

Response:
As said above we corrected the significance values according to the multiple comparisons.

We decided not to perform a multivariate analysis first of all because of our cross-sectional design. Furthermore we did not pre-define specific potential confounders and the sample size would have been too small. Our study results can therefore only be interpreted as the results of an exploratory study.

Because of your advice, we investigated additionally if the median scores of the questionnaires assessing self-perceived disability, anxiety and depression differ significantly between the different groups of diagnoses, illness duration, living condition and employment status. This was not the case. We investigated secondly the associations between the above mentioned categorical variables and the dichotomous variables of disability, anxiety and depression. The last analyses we performed in the total sample as well as in both genders. None of the tests was significant. These results might reduce the concern that the variables diagnostic group, illness duration, living condition, and employment status might confound the associations between self-rated severe disability and abnormal anxiety and depression.

Comment (14) Results
The description of the results and the tables correspond to an exploratory analysis, which could be summarized. However, the multivariate analysis, including potential confounders, would be essential to confirm any finding.

Response:
As mentioned above you are right that we performed purely an exploratory study. We adapted the sections statistical analyses and results as well as the tables by adding some of the information you missed and deleting less relevant information: We decided to report only the prevalence rates of abnormal anxiety/depression based on the recommended cut-off criteria of the German version of the HADS. We restricted the report of symptom severity.

Comment (15) Discussion
(15.1) The contribution of confounding factors should be discussed after a complete analysis is performed, considering the available literature.
(15.2) The limitations of the study are not fully described (eg. the instrument selected to assess depression cannot differentiate depressive states, the power of the study to test all the comparisons and correlations).

Response:
(15.1) In our response to your comment (13) we tried to explain why we did not perform multivariate analyses. But because of your advice we completed the list
of potential confounding factors in the discussion section and attached references per each factor

(15.2)
We adapted the discussion section according to your advices.

Comment (16) Conclusion
The conclusions are only partially supported by the study.

Response/Question
We adapted the conclusion and added the advice of the need of further surveys (p16/17).

Comment (17) Abstract
The abstract may have to be modified accordingly.

Response: We did it.