Author's response to reviews

Title: Stress matters! Psychophysiological and emotional loadings of fetal magnetic resonance imaging

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Author's response to reviews: see over
Reviewer 1:

In the current study, the authors aimed to explore the emotional and psychophysiological reactions of pregnant women undergoing fetal MRI. 60 women were prospectively evaluated using standardized measures of anxiety, emotional states and depressive symptoms. They found significantly differences in fast and slow physiological stress measures between women with and without a supporting person accompanying them to the examination. Furthermore, women with well-marked stress coping strategies experienced lower levels of stress during the examination. The topic of the study is original and shows how fetal MRI assessment should be tailored and an appropriate counselling provided in order to avoid unnecessary parental anxiety.

The statistical analysis is appropriate, the conclusions in line with the results and the manuscript generally well written.

I would therefore recommend it for publication in the journal and I have only minor queries that should be address.

We thank the reviewer for this very positive feedback.

- The authors did not find any significant impact of severity of diagnosis on stress responses. However, the three categories are not well described in the manuscript. I think that adding a supplementary table showing the different anomalies in the three groups might help in understanding why there was no difference in the stress response among the different groups.

We thank the reviewer for this important comment. In the revised version of the manuscript a more detailed description on the referring diagnosis was included (Methods section, pages 5-6).

“The subjects were classified due to the severity of previous ultrasound using three different categories: no fetal malformation (group 1), fetal pathology compatible with survival (group 2), and fetal pathology probably not compatible with survival (group 3) [24] (group 1: 10 subjects, no fetal malformation; group 2: 35 patients in total, mildly enlarged ventricles (no identifiable cause, n=9), enlarged cisterna magna (no identifiable cause, n=2), mild IUGR (n=5), skeletal pathologies (cleft lip and palate (n=4), clubfoot (n=1), micrencephaly (n=1)), unilateral kidney pathologies (hydronephrosis (n=4), multicystic kidney (n=1), diaphragmatic hernia (contralateral lung volume normal, n=2), CCAM (n=2), gastrochisis (n=2), partial CCA (n=1), polyhydramnios (no identifiable cause, n=1); group 3: 15 patients in total, large menigomyelocele (n=1), complex congenital heart defects (n=6), stillbirths (n=4), large fetal tumors (n=2), massive hydrocephalus (n=1), large spina bifida (n=1)).”

- Do the authors have any information regarding the maternal stress response in case fetal MRI change the diagnosis of the scan? It would be interesting to know the maternal stress response in case of a false positive US diagnosis (MRI negative). This would highlight the need for tailoring fetal MRI.

Unfortunately, we were not able to assess the mother’s stress response after they received the diagnosis. The reason for which is, that mothers’ are informed by their referring physician and not necessarily by the performing radiologist. This important point was added in the revised version of the manuscript (Discussion section, page 14).
“It would have been of great interest to compare maternal stress response after confirmation or exclusion of the fetal diagnosis after the MRI investigation. As patients are informed about the diagnosis of the MRI examination not immediately after the procedure but by their referring physician, this was not possible in the reported study, but should be investigated in future studies.”

• The authors performed an inter-group comparison for several characteristics, such as the presence of an accompanying person, type of anomaly etc. Was logistic regression analysis used to assess whether these characteristics were independently associated with higher stress responses?

We did not perform logistic regression analysis, due to differing subgroup sizes.

• Tables 1 and 3 should be re-formatted and the p-value provided for each category.

We thank the reviewer for this advice and both tables were re-formatted and include p-values now (Table 2 and 4 in the revised version of the manuscript).

Reviewer 2:

Major Compulsory Revisions
1. Further clarity is needed regarding group 1. The risk that is 'suspected', needs to be explored to gain an understanding of what this group represents? Are they intended to be a control group or a group with unclear lesions with uncertain clinical significance? This changes the nature of the group entirely.

We thank Reviewer 2 for this important comment. The assignment to the three groups was performed based on a previous study performed by our group (Leithner, K., Pörnbacher, S., Assem-Hilger, E., Krampl-Bettelheim, E., and Prayer, D. (2009). Prenatal magnetic resonance imaging: towards optimized patient information. Ultrasound Obstet. Gynecol. 34, 182–7. doi:10.1002/uog.6391). In this study patients were categorized upon their referral diagnosis. As also pointed out by Reviewer 1, more information on the three groups is needed. Therefore, we included detailed information on the referring diagnosis in the revised version (Methods section, pages 5-6).

“Subjects were classified due to the severity of previous ultrasound using three different categories: no fetal malformation (group 1), fetal pathology compatible with survival (group 2), and fetal pathology probably not compatible with survival (group 3) [24] (group 1: 10 subjects, no fetal malformation; group 2: 35 patients in total, mildly enlarged ventricles (no identifiable cause, n=9), enlarged cisterna magna (no identifiable cause, n=2), mild IUGR (n=5), skeletal pathologies (cleft lip and palate (n=4), clubfoot (n=1), micorcephaly (n=1)), unilateral kidney pathologies (hydronephrosis (n=4), multicystic kidney (n=1), diaphragmal hernia (contralateral lung volume normal, n=2), CCAM (n=2), gastrochisis (n=2), partial CCA (n=1), polyhydramnios (no identifiable cause, n=1); group 3: 15 patients in total, large menigomyelocele (n=1), complex congenital heart defects (n=6), stillbirths (n=4), large fetal tumors (n=2), massive hydrocephalus (n=1), large spina bifida (n=1)).”
2. Clarity is needed regarding the information given to mothers prior to the scan, patient leaflets for example, or video links. How the statistics were calculated for this is not clear. Were the measures standardised? Was it noted whether the mothers had had a previous MRI for other reasons? This would be important.

It was not assessed if mothers had previous MRI examinations for other reasons but five out of 63 mothers have already been to a fetal MRI examination. This was included in the revised version of the paper. In the socio-demographic questionnaire we assessed how referred mothers were informed before they came to our institution (patient leaflet or by a physician, or both). In the revised version of the manuscript we included a table for more information (see new table 1 for details).

Table 1: Descriptive information on how mothers were informed about the fetal MRI measurement prior to their visit. Regardless of the information status, mothers received information on the procedure by a medical professional immediately before the scanning session.

<table>
<thead>
<tr>
<th>Informed by</th>
<th>MRI leaflet</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Referring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>n</td>
<td></td>
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<tr>
<td>%</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>n</td>
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<td>%</td>
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</tbody>
</table>

3. Clarity would be needed regarding the inherent stresses related to the MRI scan i.e. claustrophobia and whether a patient had previously had an MRI scan.

We agree with the reviewer that this is important information. Regarding claustrophobia, we did not include any mothers that described claustrophobic symptoms as this would surely bias the stress response irrespective of referring diagnosis and whether the mother was accompanied or not. As pointed out above five of the 63 females have already undergone a fetal MRI scan. As these five were distributed across all three referral groups we did not look for specific effects. But looking at their subjective and physiological stress response did not show a significantly diminished stress reaction, thus they were as stressed as the pregnant women who underwent their first MRI scan.

4. The technical matters regarding why the SCL measures were not possible needs to be explained.
   Line 176.

We are sorry for the missing information and added this to the revised version. For SCL measures we could not use all measurements due to problems with the electrode and the recording device; and
for the cortisol probes not all samples could be used due to an insufficient amount of saliva. This was included in the revised version of the manuscript (Results section, page 7).

“Due to technical matters (broken finger electrode) SCL measures were acquired from 37 females. Moreover, due to insufficient amount of saliva complete saliva samples were collected from 58 females.”

5. It must be clear from the title and tone of the paper that the purpose of this article is to look at the immediate psychological response within the mother, and not indicating a negative outcome for the fetus. Identifying a reduction in stress with addition of a supportive person is of benefit, but it must be clear that the stress related to MRI is not investigated in this paper with regard to adverse fetal outcomes. It would also be helpful to comment on the effect after mothers receive the MRI report and if stress levels are changed by this.

We agree with the reviewer that in the current study we solely focused on the stress response within the mothers undergoing fetal MRI. We did not collect information whether and how this procedure affected the fetus. Moreover, we also did not assess stress levels after mothers received the MR report – as this sometimes takes up to several days until the patients are informed by their referring gynecologist. To follow the reviewer’s advice we changed the title into “Stress matters! Psychophysiological and emotional loadings of pregnant women undergoing fetal magnetic resonance imaging.” Moreover, we added a paragraph on future studies that should also assess stress reactions after mothers received the MR report in the revised version of the manuscript (Discussion section, page 14).

“It would have been of great interest to compare maternal stress response after confirmation or exclusion of the fetal diagnosis after the MRI investigation. As patients are informed about the diagnosis of the MRI examination not immediately after the procedure but by their referring physician, this was not possible in the reported study, but should be investigated in future studies.”