Fully Automated Subtraction of Heart Activity (FAUNA) for Fetal Magnetoencephalography Data*

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***Abstract*— Fetal magnetoencephalography (fMEG) is a method to record human fetal brain signals in pregnant mothers. Nevertheless the amplitude of the fetal brain signal is very small and the fetal brain signal is overlaid by interfering signals mainly caused by maternal and fetal heart activity. Several methods are used to attenuate the interfering signals for the extraction of the fetal brain signal. However currently used methods are often affected by a reduction of the fetal brain signal or redistribution of the fetal brain signal. To overcome this limitation we developed a new fully automated procedure for removal of heart activity (FAUNA) based on Principal Component Analysis (PCA) and Ridge Regression. We compared the results with an orthogonal projection (OP) algorithm which is widely used in fetal research. The analysis was performed on simulated data sets containing spontaneous and averaged brain activity. The new analysis was able to extract fetal brain signals with an increased signal to noise ratio and without redistribution of activity across sensors compared to OP. The attenuation of interfering heart signals in fMEG data was significantly improved by FAUNA and supports fully automated evaluation of fetal brain signal.**

I. INTRODUCTION

Fetal magnetoencephalography (fMEG) allows the non invasive recording of maternal and fetal heart signals and spontaneous [1], [2], and event related brain activity [3], [4], [5], [6], [7], [8] of the fetus with good spatio-temporal resolution. The analysis of fetal brain signals makes it possible to address important questions regarding the developmental process of the fetal brain and the autonomic nervous system [9] as well as the maternal influence on the metabolic and cognitive outcome of neonates.

The evaluation of fetal brain activity is challenging since the brain signal is superimposed by fetal and maternal heart activity, which have a signal strength 10-1000 times larger than the fetal brain signal. Thus, it is mandatory to remove this heart activity before the analysis of fetal brain activity. The detailed characterization of the interfering sources is only possible with multisensor systems covering larger parts of the maternal abdomen. A widely used method for heart artifact removal in fMEG data is Orthogonal Projection (OP) [10], [11]. OP separates heart activity from other activity in a dataset by attenuation of the estimated signal space of the heart signal. This process is fairly effective in removing the maternal and in most cases also the fetal heart signals but it has its limitations. One drawback of the method is a possible redistribution of the signal [12], which can lead to inconsistent localization and involves the risk that some brain activity is removed together with the heart signals. Since the fMEG signal is only present in a small number of sensors, the identification of these sensors has to work reliably to make further automated evaluation steps possible.

To improve the analysis of fetal brain activity and open up new possibilities for advanced analysis methods, the aim of this work was to develop a fast and effective artifact rejection procedure that does not cause signal redistribution. This algorithm for **f**ully **au**tomated subtractio**n** of heart **a**ctivity is abbreviated FAUNA. In the following sections we describe the algorithm and its evaluation based on a model for artificial fMEG.

II. METHODS

We first explain how the proposed algorithm works step by step. Subsequently we compare it to the current standard method and verify its functionality.

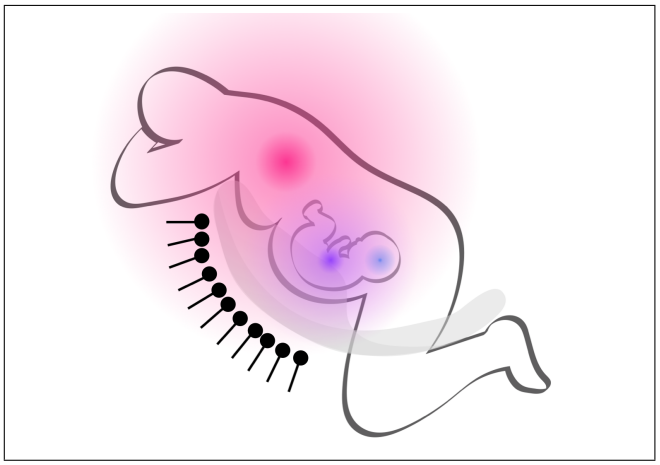

Fig. 1. Sketch of a pregnant woman on the fMEG device. Sensors (black) record maternal heart (red) fetal heart (purple) and fetal brain activity (blue).

*This work was partially supported by the Luminous project (EU-H2020-FETOPEN GA No.686764) and grant (01GI0925) from the Federal Ministry of Education and Research (BMBF) to the German Center for Diabetes Research (DZD e.V.).

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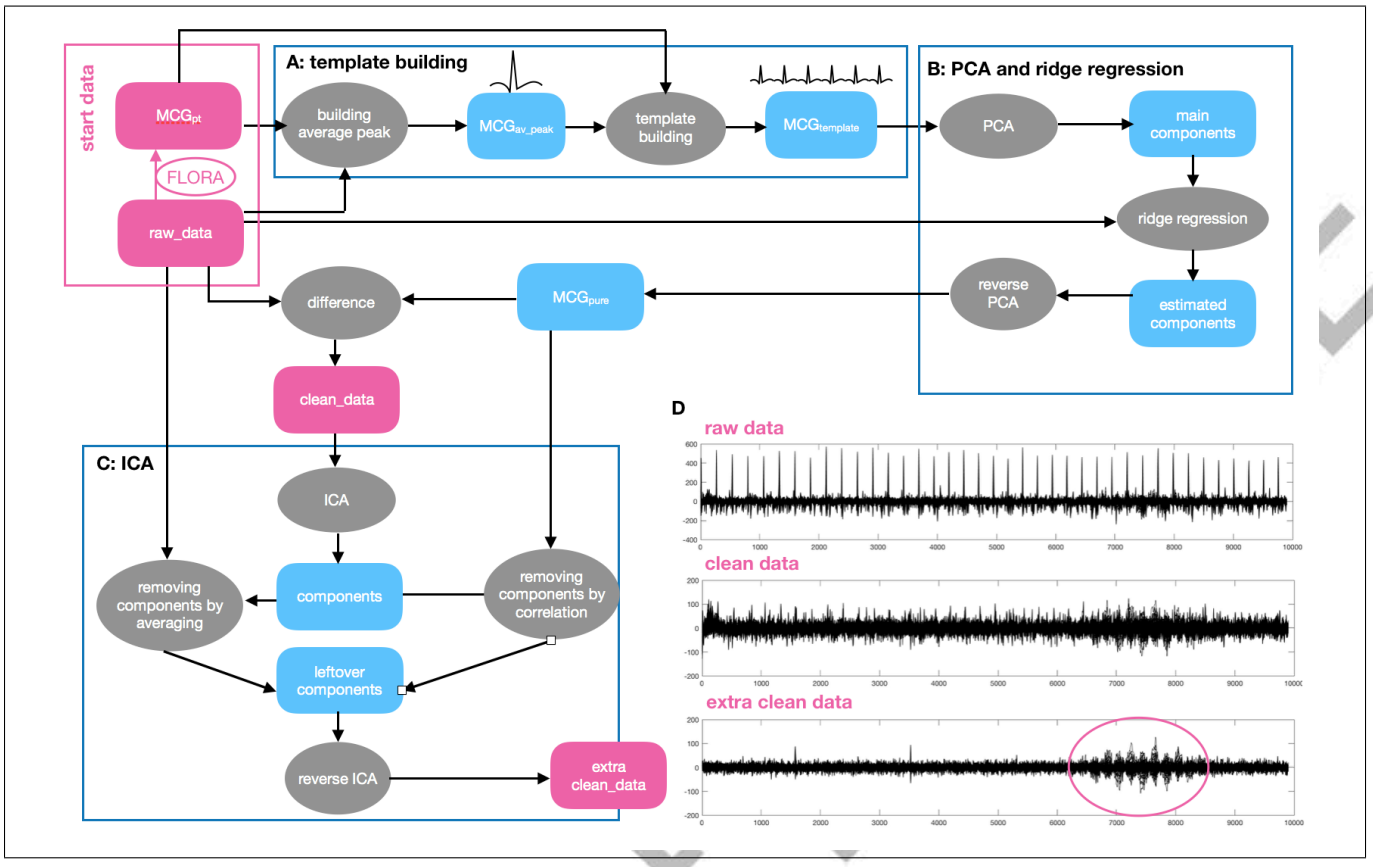

Fig. 2. Schematic display of FAUNA algorithmic structure. Starting with the raw data and the peak times of the R-peaks (MCG_{pt}), FAUNA consists of three steps: A) Building a heart beat template, B) PCA and Ridge regression and C) the ICA refinement. The procedure is, with a few exceptions, the same for maternal and fetal heart signals. D: Short time sequence of the data before, during and after the removal of the fetal MCG signal. After the removal the triggered brain signal is visible (red circle).

A. FAUNA

FAUNA is an algorithm for fully automated subtraction of heart activity to prepare fMEG data for further processing. For a subtraction of the heart signals from a fMEG dataset, it is necessary to estimate a clear heart signal first. This procedure is done twice in a row for fetal datasets to remove the maternal and fetal heart activity and one time for neonatal datasets to remove the heart activity of the newborn.

Before the heart activity removal can be performed, a detection of the R-peaks is necessary. FAUNA uses the result of an external automated R-peak detection algorithm (FLORA, [13]) which is used for maternal and fetal R-peaks. In the first step, the peak times of these R-peaks are used to generate a template of the heart activity. By using average heart beats for the template the risk of removing anything else than the heart activity is minimized. In the second step several components of the heart activity are selected and estimated on the original dataset and removed afterwards. The last step divides the remaining signal into independent components and additionally removes the components that correlate with the heart activity.

An overview of the different steps of FAUNA is shown in Figure 2. The different steps are described in the following:

1) Building a heart beat template: The raw dataset is filtered using a second order butterworth filter from 1-35 Hz. Thereafter an average heartbeat is built using the average over the R-peaks (MCGpt) for each sensor. By concatenating this average heart beat template with the distance of the original R-R intervals, an artificial pure heart signal is built for each sensor (see Fig. 2 A).

2) PCA and Ridge regression: As a static template does not take into account signal variations, we create a model for generating a dynamic template that takes into account these variations. To reduce noise in the data and the dimensionality of the data, a Principal Component Analysis (PCA) is performed on the artificial heart signal and the 4 main components are selected (3 main components for fetal heart). To build a model that takes into account signal variations, a ridge regression is trained to estimate these 4 components based on the original dataset. For each component, a separate ridge regression is trained. The resulting ridge regression models serve as a spatial filter [14], which is a linear combination of all input sensors, with the aim to extract the heart component as close to the template as possible, while reducing noise and all other activity that is not related to that component. The spatial filter thereby allows to extract the heart components from the MEG signal with a good signal-to-noise ratio. In contrast to a template-based approach,

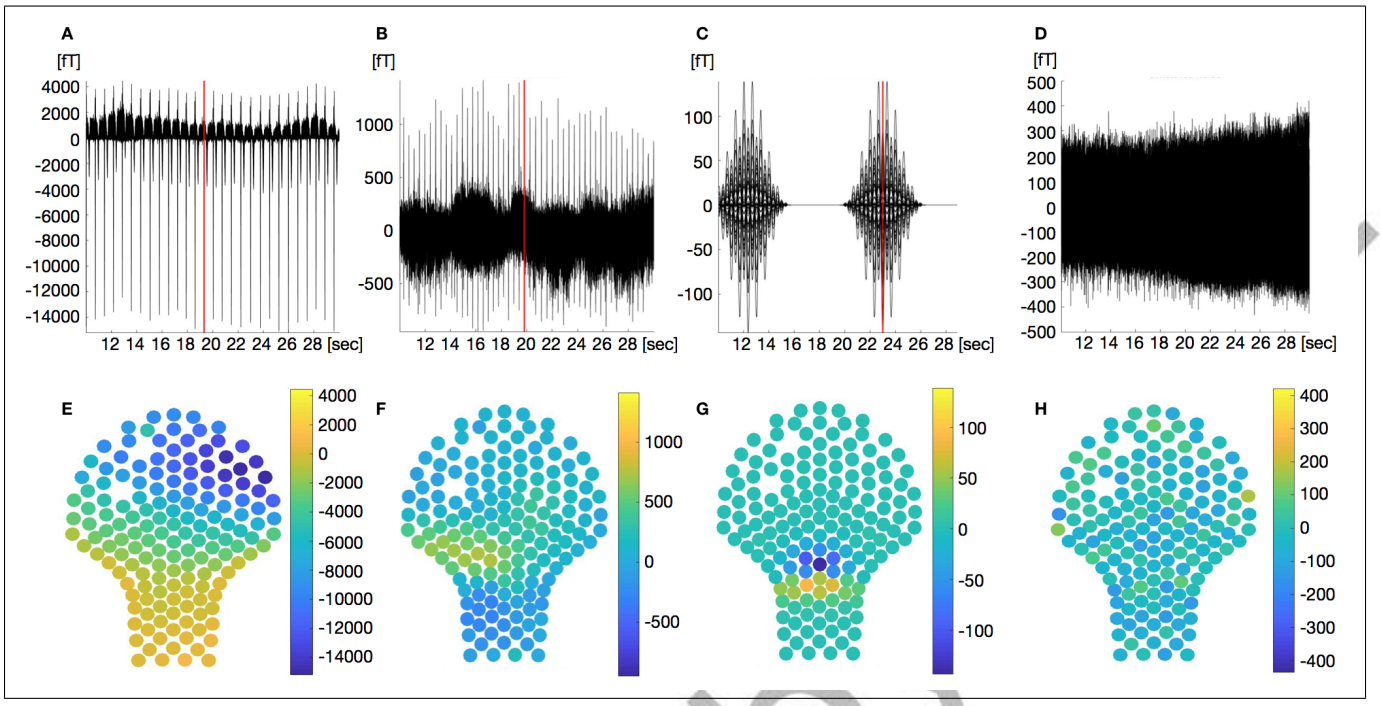

Fig. 3. The first row shows the magnetic activity, averaged over all sensors, in an segment of 20 sec duration for A) maternal heart, B) fetal heart, C) fetal brain and D) noise. The second row represents the magnitude of all sensors at the time point of the red line for E) maternal heart, F) fetal heart, G) fetal brain and H) noise.

extracting the heart components by a spatial filter has the benefit that dynamic variations of the heart components are accounted for. As the heart components are also modeled for the time points where the R-peak detection failed to detect a peak, those peaks can be visible in the spatially filtered signal and can be used to fill up missing R-peaks. Afterwards, the heart components extracted by the spatial filters are used for a reverse PCA to transform the estimated heart components back to a dynamic estimation of the heart signal for all sensors (see Fig. 2 B).

This pure estimated heart signal is then subtracted from the original dataset.

3) ICA refinement: Since the former procedure removes a large amount but not all heart signal components, in the next step an additional independent component analysis (ICA) is performed on the resulting dataset. First, the correlation of each component and the pure heart signal is calculated and second, the average of each component at the R-peak time points is generated. 40% of the components with the highest correlation and average components that reach a threshold of 1 were also removed from the remaining dataset. By reversing the ICA with the leftover components, the dataset without interfering heart activity is generated (see Fig.2 C).

B. Model

A model with real and simulated data was used. Real data were collected by a 156 sensor system (SARA, SQUID Array for Reproductive Assessment, VSM MedTech Ltd., Port Coquitlam, Canada) at the University of Tübingen with a sampling rate of 610 Hz. The model data were adapted to this system and sampling rate.

To evaluate the quality of heart removal by FAUNA, we compared it to Orthogonal Projection (OP). As the real fetal brain activity is unknown in real datasets and the aim is to extract the fetal brain activity as well as possible, we do not have a ground-truth of the fetal brain activity in a real dataset. Therefore we combined artificially generated fetal brain activity with real fMEG data. We generated a dataset consisting of real fMEG background activity and heart signals, generated artificial fMEG data based on a forward model [15] and superimposed that artificial fMEG data by real maternal magneto-cardiography (mMCG) signals, real fetal magneto-cardiography (fMCG) signals and real background noise. To extract these real mMCG and fMCG signals for the model, a dataset was selected where an independent component analysis (ICA) could separate multiple mMCG and fMCG components. An reverse ICA was performed on six mMCG components and on two fMCG components to generate the maternal (Fig. 3 A,E) and fetal heart signal (Fig. 3 B,F) included in the model. The artificial fetal brain signal was put into the time trace at specific trigger time points (see Fig. 3 C,G). Triggers were set with a random distance of 10-15 sec. An empty fMEG measurement was performed to generate the background noise (Fig. 3 D,H).

After generating an artificial dataset with this model, the generated dataset was processed by OP and FAUNA.

C. Evaluation

The evaluation of fMEG signals is usually made over the whole time course of a recording or on data averaged over a specific trigger. To cover both options we analyzed some of our evaluation parameters first over the whole recording

time and second on data averaged over all fMEG simulation triggers.

1) Redistribution analysis (RMSE over sensors): To compare the redistribution of the brain signal over the sensors we calculated the RMSE (root-mean square error) for each sensor, of the difference between the modeled brain signal and the datasets after processing with OP and FAUNA, over the whole recording time. We compared the RMSE over all sensors as well as for the 10 sensors where the magnitude of the simulated brain signal was the highest.

2) Correlation analysis (CORR): To evaluate how much of the simulated brain signal is left in the data after the removal of maternal and fetal heart signals, the correlation coefficient (CORR) between the simulated brain signal, and the remaining data is calculated. This calculation is done on the whole time course and on data averaged over all fMEG simulation triggers.

3) Signal to noise ratio (SNR): The SNR was calculated by dividing the RMS of the simulated brain signal ($fMEG_{sim}$) by the RMS of the difference between the simulated brain signal ($fMEG_{sim}$) and the remaining signal $fMEG_{rest}$) after the heart artifact removal for both methods (OP and FAUNA) and each sensor, for the whole time course as well as for the data averaged over all fMEG simulation triggers. $SNR = RMS(fMEG_{sim})/RMS(fMEG_{rest} - fMEG_{sim})$

4) Statistics: Results from all above mentioned metrics were compared for OP and FAUNA by using a Wilcoxon Signed Rank Test. This comparison was done for spontaneous fMEG activity and fMEG activity averaged over all fMEG simulation triggers. 3 sensors were excluded within preprocessing with FLORA [13] and thus were excluded for statistical comparison in all methods to have an equivalent number of sensors. Results are reported in [mean ± standard deviation].

III. RESULTS

A. Redistribution analysis (difference in RMSE over sensors)

A comparison of the RMSE for all sensors resulted in significant ($p < 0.001$) lower values for FAUNA [1.26±0.23] than for OP [1.38±0.13] (see Fig. 4 A-D).

Comparing the RMSE only for the 10 sensors with the highest RMS of the simulated fMEG signal showed also a significant difference (p=0.019531) between OP [1.00±0.16] and FAUNA [0.67±0.10] (see Fig. 4 A-C red circles and E). The RMSE here is also significantly lower for FAUNA.

B. Correlation analysis

A comparison of fMEG CORR over the whole time course showed a significant difference ($p < 0.001$) between OP [0.11±0.13] and FAUNA [0.21±0.22] (see Fig. 5 A-C,G).

Comparing fMEG CORR for the averaged data also showed a significant difference ($p < 0.001$) between OP [0.50±0.30] and FAUNA [0.69±0.28] (see Fig. 5 D-F, H). CORR is significantly higher for FAUNA in both cases.

C. Signal to noise ratio (SNR)

A comparison of fMEG SNR over the whole time course for all sensors showed a significant difference ($p < 0.001$) between OP [0.09±0.21] and FAUNA [0.25±0.47] (see Fig. 6 A).

A comparison of fMEG SNR on the averaged dataset

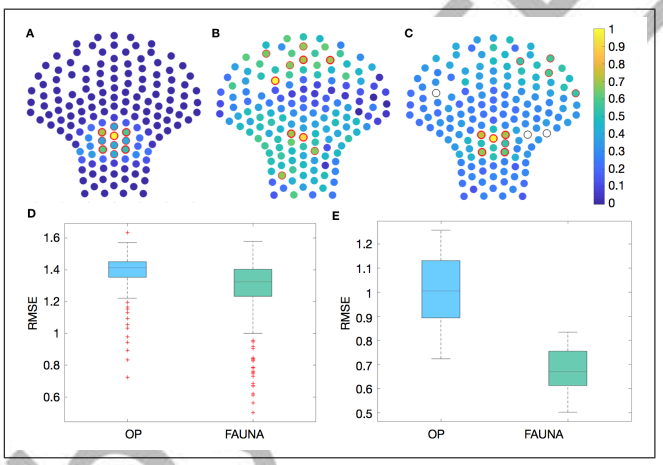

Fig. 4. First row: The normalized RMS over the whole recording time for all sensors for A) the simulated signal, B) the signal after processing heart activity removal with OP and C) the signal after processing heart activity removal with FAUNA. The sensors with the 10 highest RMS values are marked with a red circle, top 5 with a bold red circle. Second row: Boxplot of the RMSE between the actual fetal brain activity and the reconstructed signal by either OP or FAUNA for D) all sensors E) 10 sensors with highest RMS of the simulated fMEG signal.

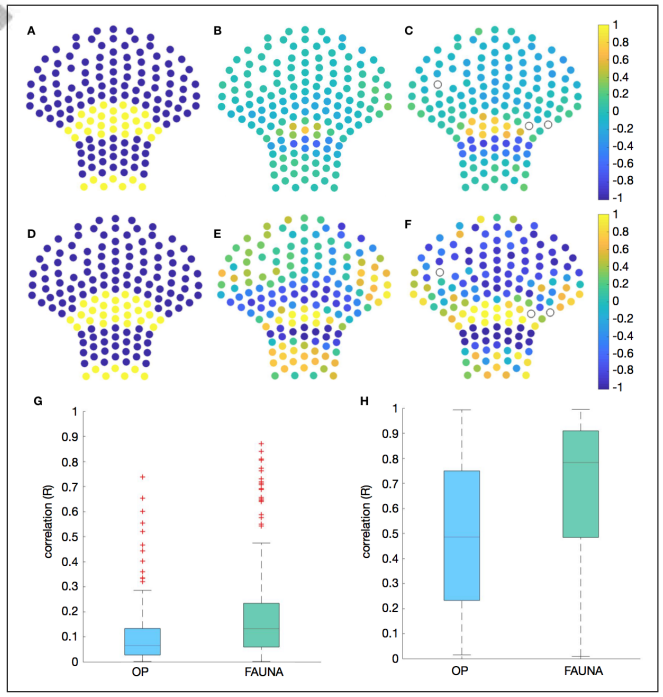

Fig. 5. First row: Correlation of the original fMEG signal over the whole recording time for A) simulated signal B) OP C) FAUNA. Second row: Correlation between the original fMEG signal averaged over all fMEG simulation triggers for D) simulated signal E) OP F) FAUNA. Third row: Boxplot of the correlation with the original fMEG signal for all sensors over G) the whole time of the recording and H) data averaged over all fMEG simulation triggers.

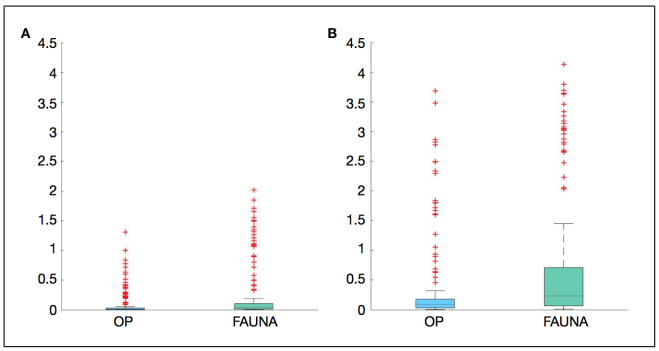

Fig. 6. Boxplot of SNR for all sensors over A) whole time measurement and B) data averaged over all fMEG simulation triggers.

for all sensors showed a significant difference ($p < 0.001$) between OP [0.50±1.10] and FAUNA [0.78±1.20] (see Fig. 6 B).

SNR is significantly higher for FAUNA in both cases.

IV. CONCLUSIONS

Orthogonal Projection (OP) until now is a well established method for heart activity removal in fMEG data. In this work we introduced our new algorithm for **f**ully **au**tomated subtractio**n** of heart **a**ctivity (FAUNA) and compared both methods by using a model of real heart and simulated brain activity to evaluate both methods on completeness and redistribution. Therefore, we used the root mean square error (RMSE), the correlation coefficient (CORR) and the signal to noise ratio (SNR) as measures.

The significantly higher CORR values between FAUNA and the simulated signal showed that more brain signal is left after heart artifact removal with FAUNA than between OP and the simulated signal.

This indicates that by using methods based on orthogonal projection, some brain signal is removed together with the heart signal and not only redistributed. The impact of the redistribution is visible when looking at the RMSE for all sensors. The remaining fMEG signal after heart artifact removal with FAUNA shows a cluster of high RMS amplitudes in the same region where the original simulated fetal brain signal was located. Also 5 of the 10 sensors with the highest RMS amplitudes are the same. In the remaining fMEG signal after artifact removal with OP there is no cluster visible and only two of the five sensors with highest RMS are congruent with the simulated fetal brain signal (see Fig. 4 A-C). The findings from the RMSE support these observations, showing a significantly lower difference for FAUNA. The SNR over all sensors is significantly higher for FAUNA, compared to OP, for spontaneous and averaged brain activity. This is in accordance with the findings from the correlation, which showed that with FAUNA there is more brain signal left in general.

In conclusion, we developed and tested a new algorithm (FAUNA) for the removal of heart artifacts from fMEG data. Compared to a well established method, FAUNA provides better results in terms of SNR and does not have the drawback of a redistributed signal. As FAUNA is also fully automated, it is a superior alternative to currently used methods for removal of heart signals. Using FAUNA for heart artifact removal, the remaining signal containing fetal brain activity in normal datasets should form clusters of high RMS values, even for spontaneous brain activity. Such RMS clusters can easily be identified by automated procedures.

REFERENCES

[1] D. F. Rose and H. Eswaran, "Spontaneous neuronal activity in fetuses and newborns," *Experimental neurology*, vol. 190, pp. 37–43, 2004.

[2] N. Haddad, R. B. Govindan, S. Vairavan, E. Siegel, J. Temple, H. Preissl, C. L. Lowery, and H. Eswaran, "Correlation between fetal brain activity patterns and behavioral states: an exploratory fetal magnetoencephalography study," *Experimental neurology*, vol. 228, no. 2, pp. 200–205, 2011.

[3] M. Chen, B. D. Van Veen, and R. T. Wakai, "Linear minimum mean-square error filtering for evoked responses: Application to fetal meg," *IEEE transactions on biomedical engineering*, vol. 53, no. 5, pp. 959–963, 2006.

[4] R. Draganova, H. Eswaran, P. Murphy, C. Lowery, and H. Preissl, "Serial magnetoencephalographic study of fetal and newborn auditory discriminative evoked responses," *Early human development*, vol. 83, no. 3, pp. 199–207, 2007.

[5] L. Moraru, R. Sameni, U. Schneider, J. Haueisen, E. Schleußner, and D. Hoyer, "Validation of fetal auditory evoked cortical responses to enhance the assessment of early brain development using fetal meg measurements," *Physiological measurement*, vol. 32, no. 11, p. 1847, 2011.

[6] J. Muenssinger, T. Matuz, F. Schleger, R. Draganova, M. Weiss, I. D. Kiefer-Schmidt, A. Wacker-Gussmann, R. B. Govindan, C. L. Lowery, H. Eswaran *et al.*, "Sensitivity to auditory spectral width in the fetus and infant–an fmeg study," *Frontiers in human neuroscience*, vol. 7, p. 917, 2013.

[7] F. Schleger, K. Landerl, J. Muenssinger, R. Draganova, M. Reinl, I. Kiefer-Schmidt, M. Weiss, A. Wacker-Gußmann, M. Huotilainen, and H. Preissl, "Magnetoencephalographic Signatures of Numerosity Discrimination in Fetuses and Neonates," *Developmental Neuropsychology*, vol. 39, no. 4, pp. 316–329, may 2014.

[8] K. Linder, F. Schleger, I. Kiefer-Schmidt, L. Fritsche, S. Kümmel, M. Heni, M. Weiss, H.-U. Häring, H. Preissl, and A. Fritsche, "Gestational Diabetes Impairs Human Fetal Postprandial Brain Activity," *The Journal of Clinical Endocrinology & Metabolism*, vol. 100, no. 11, pp. 4029–4036, nov 2015.

[9] H. Preissl, C. L. Lowery, and H. Eswaran, "Fetal magnetoencephalography: current progress and trends," *Experimental neurology*, vol. 190, pp. 28–36, 2004.

[10] J. McCubbin, S. E. Robinson, R. Cropp, A. Moiseev, J. Vrba, P. Murphy, H. Preissl, and H. Eswaran, "Optimal reduction of MCG in fetal MEG recordings," *IEEE Transactions on Biomedical Engineering*, 2006.

[11] J. D. Wilson, R. B. Govindan, J. O. Hatton, C. L. Lowery, and H. Preissl, "Integrated approach for fetal QRS detection," *IEEE Transactions on Biomedical Engineering*, vol. 55, no. 9, pp. 2190–2197, 2008.

[12] J. Vrba, S. E. Robinson, J. McCubbin, P. Murphy, H. Eswaran, J. D. Wilson, H. Preißl, and C. L. Lowery, "Human fetal brain imaging by magnetoencephalography: Verification of fetal brain signals by comparison with fetal brain models," *NeuroImage*, 2004.

[13] K. Sippel, J. Moser, F. Schleger, H. Preissl, W. Rosenstiel, and M. Spueler, "Fully automated r-peak detection algorithm (flora) for fetal magnetoencephalographic data," *Computer Methods and Programs in Biomedicine, submitted (minor revision)*, 2019.

[14] M. Spüler, "Spatial filtering of eeg as a regression problem," in *7th Graz Brain-Computer Interface Conference*, 09 2017.

[15] J. C. Mosher, R. M. Leahy, and P. S. Lewis, "Matrix kernels for meg and eeg source localization and imaging," in *Acoustics, Speech, and Signal Processing, 1995. ICASSP-95., 1995 International Conference on*, vol. 5. IEEE, 1995, pp. 2943–2946.

Citation: K. Sippel et al., "Fully Automated Subtraction of Heart Activity for Fetal Magnetoencephalography Data*," 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany, 2019, pp. 5685-5689, doi: 10.1109/EMBC.2019.8856603;
Link: https://ieeexplore.ieee.org/document/8856603