Automated Detection of Fetal Brain Signals with Principal Component Analysis*

Julia Moser[1], Katrin Sippel[1], Franziska Schleger[1] and Hubert Preißl[1,2]

***Abstract*— Detection of fetal brain signals in fetal magnetoencephalographic recordings is – due to the low signal to noise ratio – challenging for researchers in this field. Up to now, state of the art is a manual evaluation of the signal. To make the evaluation more reproducible and less time consuming, an approach using Principal Component Analysis is introduced. Locations of the channels of most importance for the first three principal components are taken into account and their possibility of resembling brain activity evaluated. Data with auditory stimulation are taken for this analysis and trigger averaged signals from the channels selected as brain activity (manually & automatically) compared. Comparisons are done with regard to their average baseline activity, activity during a window of interest and timing and amplitude of their highest auditory event-related peak. The number of evaluable data sets showed to be lower for the automated compared to manual approach but auditory event-related peaks did not differ significantly in amplitude or timing and in both cases there was a significant activity change following the tone event. The given results and the advantage of reproducibility make this method a valid alternative.**

I. INTRODUCTION

How much does a fetus in the womb already process from the outside world and how does the developing brain process this information? This is a question, that can be addressed with fetal magnetoencephalography (fMEG) which gives the opportunity to observe the developing fetal brain non-invasively [1]. With the help of this technique auditory event-related responses (AER) [2], [3], [4], [5], [6] as well as visually event-related responses [7], [8] can be investigated before birth. This is possible troughout the third trimester of pregnancy as thalamocortical connections are established between week 23 and 25 of gestation. The cochlea is developed with about 18 weeks of gestation and behavioral responses to sound are already seen and with a gestational age of 28 weeks, brain responses to sound can be observed [9], [10], [11]. In fMEG, different paradigms can be used to show phenomenons like a mismatch response [4], [12], habituation [13] or numerosity discrimination [14] in fetuses. Making fMEG a technology, which opens many possibilities for developmental neuroscience. Yet, in all those studies, localization of brain signals is a challenging endeavor due to the low signal to noise ratio in fMEG. Up to now, analysis of AERs is done manually, whereas a dipole location is chosen based on the fetal position and the channels with the highest AER selected. This makes analysis time consuming and even when following strict rules not completely reproducible among different raters. Additionally, this method is restricted to the evaluation of event-related responses and there is no equally accepted approach so far to extract brain signals for the analysis of for example frequency spectra or spontaneous brain activity. Therefore, a more automated procedure is needed to extract brain activity from fMEG data that uses different criteria then peak amplitudes. In the current paper, we present an approach to extract brain activity with a Principal Component Analysis (PCA) and additional criteria to validate plausibility of the location of brain activity.

*This work was supported by the FET Open Luminous project (H2020 FETOPEN-2014-2015-RIA under agreement No. 686764) as part of the European Union's Horizon 2020 research and training program 2014-2018.

[1]IDM/fMEG center of the Helmholtz Center Munich at the University of Tübingen, University of Tübingen, Tübingen, Germany julia.moser@student.uni-tuebingen.de

[2] Department of Pharmacy and Biochemistry; Interfaculty Centre for Pharmacogenomics and Pharma Research, Eberhard Karls University of Tübingen, 72076 Tübingen, Germany

Citation: Moser, J., Sippel, K., Schleger, F. & Preissl, H. (2019). Automated Detection of Fetal Brain Signals with Principal Component Analysis. 2019 41th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). Berlin, Germany, 2019, pp.6549-6552. doi: 10.1109/EMBC.2019.8857283; Link: https://ieeexplore.ieee.org/document/8857283

II. METHODS

A. Fetal Magnetoencephalography

fMEG uses superconducting quantum interference device (SQUID) sensors to record biomagnetic signals produced by a fetus in the womb (Fig. 1). Fetal data were recorded with a SARA (SQUID Array for Reproductive Assessment, VSM MedTech Ltd., Port Coquitlam, Canada) system installed at the fMEG Center at the University of Tübingen. To attenuate magnetic activity from the environment, it is installed in a magnetically shielded room (Vakuumschmelze, Hanau, Germany). The system includes 156 primary magnetic sensors

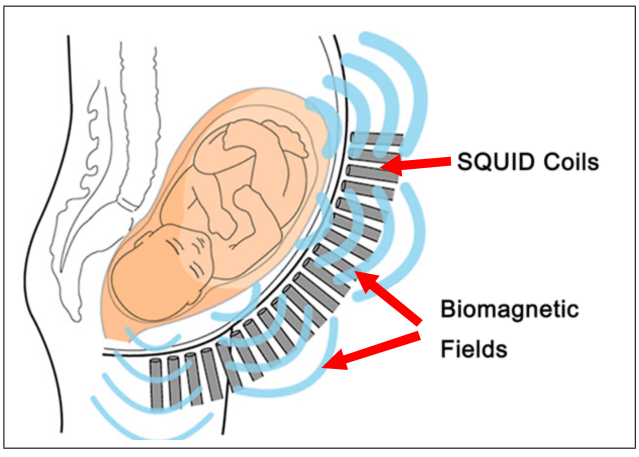

Fig. 1. Schematic drawing of fMEG measurement of biomagnetic signals

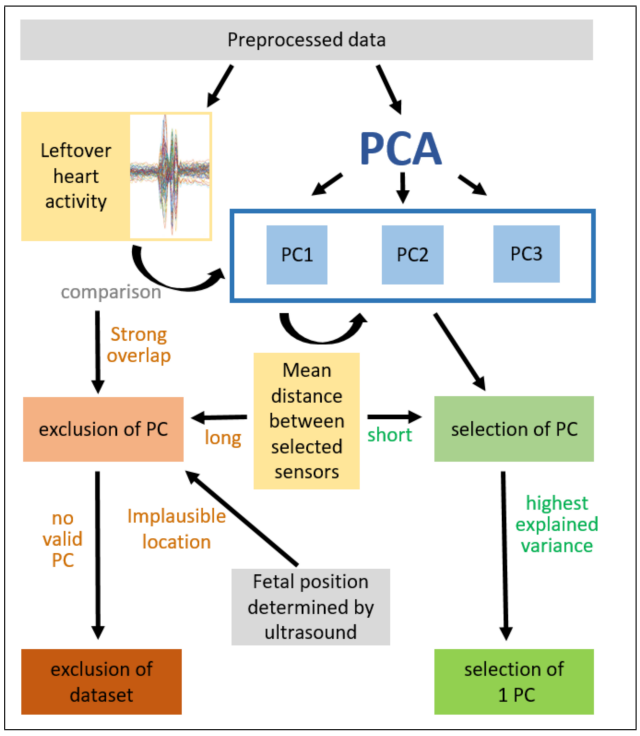

Fig. 2. Scheme of automated brain signal detection procedure including three criteria for inclusion of a signal cluster defined by a principal component

and 29 reference sensors which are distributed over a concave array, matching to the shape of the maternal abdomen. Auditory stimulation was presented via a balloon placed between the maternal abdomen and the sensor array. The fetal position was determined via ultrasound before each recording and verified afterwards.

B. Dataset

Data of the current comparative analysis, were previously analyzed in a manual fashion (for a description of the manual anlysis see [14]). 45 datasets from 45 participants were extracted from two different studies. Studies were approved by the local Ethical Committee of the Medical Faculty of the University of Tübingen, all participants gave written informed consent before participation and agreed on reuse of data for additional studies. Both studies used the same auditory paradigm, an oddball paradigm with a 500Hz standard and 750Hz deviant tone with an occurrence rate of 80% for the standard [15]. Each tone is 500ms long with an inter trial interval of 1500ms. 45 fetal recordings were selected from subjects where AER were detected, 31 recordings with a length of 10 minutes and 14 with 6 minutes. The location of the five channels with the highest AER towards the standard tone as well as the latency and amplitude of this AER were available from previous analysis. The gestational age of subjects ranges from 29 to 39 weeks.

C. Preprocessing

To be able to detect fetal brain signals, the main interfering signal sources – maternal and fetal heart activity – need to be attenuated. They are detected by pattern matching or a peak search after hilbert transformation of the signal and removed by orthogonal projection [16], [17], [18]. Data were filtered from 1-10Hz and averaged over all standard trials. Baseline correction was applied with a baseline of 200 ms before tone onset on the data up to 1000 ms after tone onset. Trials with artifacts (signals >2pT) were removed and all remaining trials averaged. Due to the different recording lengths, a mean number of 248 trials was averaged for the 31 data sets of one study and a mean of 114 trials for the other 14 data sets. As large low frequency signal drifts intervene with the proposed automated brain signal detection, filter settings were chosen slightly differently than in the previous manual evaluation (1-10Hz compared to 0.5-10Hz).

D. Automated Brain Signal Detection

For the automated detection of brain signals within the fMEG sensor space, a PCA is preformed for each subject on the 1200 ms of averaged data for all channels. It detects the principal signal components that are left after attenuation of the maternal and fetal heart, whereas it is assumed that the brain signal has to be one of the major remaining components. Therefore, the first three components are taken into account. The principal component coefficients are used to compute the location of the five sensors that strongest contribute to these components. Five sensors are selected to facilitate comparisons with previous manual analysis. These first steps result in three different sensor clusters, one representative for each component. To determine, which of the clusters best represents brain activity, three selection criteria are applied. First, the location of each cluster is compared to the fetal head position, determined by ultrasound. Clusters that are largely implausible, given this head position, are excluded. Plausibility is checked by coding head and cluster

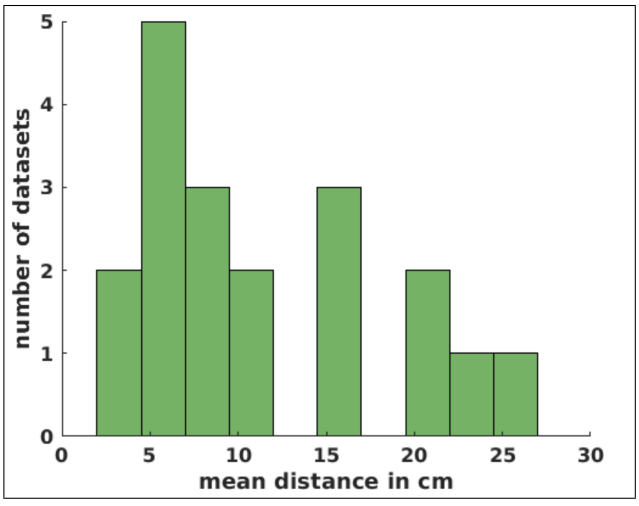

Fig. 3. Mean distance of clusters of five channels selected manually and automatically

position as in the upper or lower part of the sensor array and checking for their match. Second, the distance within the five channels of a cluster is computed and clusters that are spread over the sensor space – using a mean within distance of 10 cm as threshold – are excluded. The mean distance is calculated by calculating all distances between the five included channels and averaging over them. Third, the five channels of a cluster are compared to the leftover fetal and maternal heart signal. The amount of leftover heart signal is computed by averaging the signal at each (removed) R-peak for maternal and fetal heartbeats. For each, maternal and fetal heart leftover, the five channels with the highest amplitude at the R-peak time point are computed. If there is an overlap of more than one channel between those channels, that represent heart activity and the five channels of a cluster, the cluster is excluded. An overlap of more than one channel would signify that the heart leftover was not removed by trial averaging and the respective principal component is dominated more by heart activity than brain activity. If none of the clusters representative for the three principal components fulfill these three criteria, the dataset is not further evaluated. If more than one cluster of a dataset fulfills the above mentioned criteria, the one that belongs to the principal component that explains most variance is selected. A schematic drawing of the procedure can be seen in Fig. 2.

E. Evaluation of procedure

To evaluate the automated brain signal detection procedure, signals from the automatically detected clusters and the manually selected channels are compared. The signal used for all comparisons is the root mean square of a respective channel cluster over the 1200 ms of averaged data. As fetal AER are typically detected in a window between 100-350 ms, this window is selected as window of interest (WOI). Activity in this window is compared between the two methods as well as their activity during the baseline window (200 ms before tone onset). To quantify the AER, the difference between baseline and WOI is tested and the highest peak within the WOI selected. Peak timing as well as peak amplitude are compared between automated and manual channel selection. For this comparison, the peaks and their amplitude was detected for both, manually and automatically selected channels, as due to the slightly different filter settings, values from previous analysis were not completely matching the present data. All comparisons were done with a student t-test, p-values were adjusted for multiple comparisons by Bonferroni Correction (p=0.05/4 for the comparison of mean values and p=0.05/2 for peak timing and amplitude).

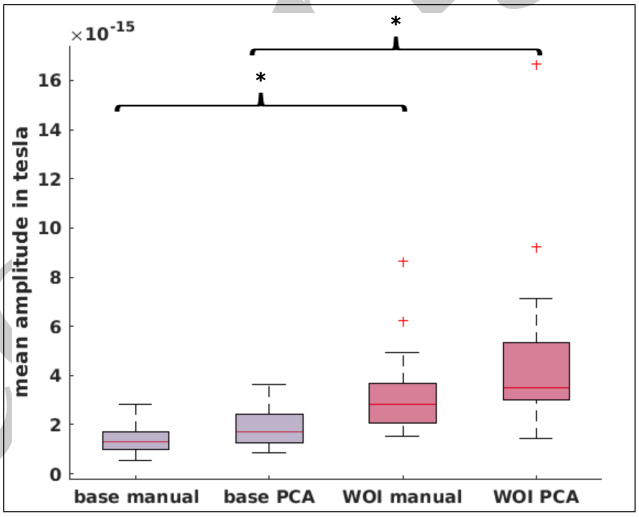

Fig. 4. Mean amplitudes in baseline window and in window of interest (WOI) for root mean square of both, manually and automatically selected channels

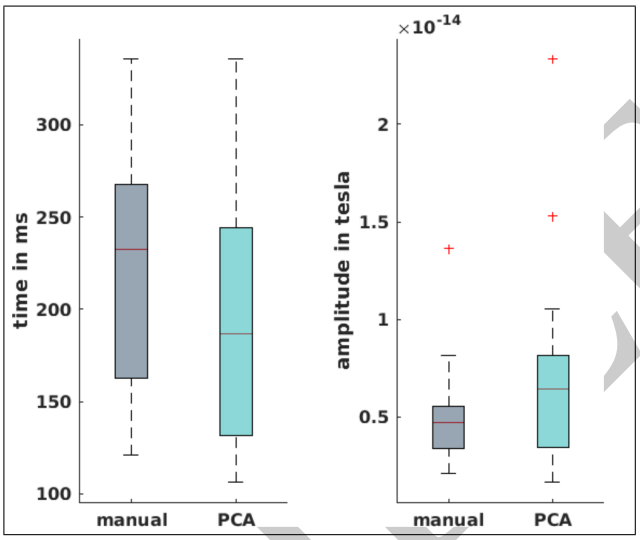

Fig. 5. Comparison of timing of highest peak in window of interest (WOI; left) and amplitude (right) between manually and automatically selected channels. Amplitudes reflect the root mean spare over five selected channels.

III. RESULTS

Automated brain signal detection was able to detect valid clusters for 19/45 data sets. Those data sets were further compared with their manually evaluated counterparts. First of all, we saw that only some of the automatically detected clusters shared a similar location with the manually selected channels with a mean distance of 11.8 cm, ranging from 3.3 to 26.7 cm (Fig. 3). Furthermore, we compared the signal resulting from the two methods. When comparing the mean activity at the baseline window, no significant difference was detected between manual and automated evaluation (manual M:1.5fT, SD: 0.6fT; automated M:1.8fT, SD: 0.7fT; p=0.028; Fig. 4). Same accounted for the comparison at the WOI (manual M:3.3fT, SD: 1.7fT; automated M:4.7fT, SD: 3.5fT; p=0.066). Yet, both evaluation methods showed a significant increase of the signal from baseline to WOI ($p<0.001$). When comparing the highest peaks in the WOI, neither their timing (manual M:219.6ms, SD 64.4ms; automated M: 191.4ms, SD:65.3ms; p=0.088) nor their amplitude (manual M:5.1fT, SD 2.7fT; automated M: 7fT, SD:5.1fT; p=0.066) showed to be significantly different (Fig. 5).

IV. CONCLUSIONS

The above presented automated brain signal detection gives the opportunity to detect fetal brain signals within the fMEG sensor space in a fast and reproducible manner. Yet, the present comparison showed, that it only yields meaningful results for a fraction of data sets. All 45 data sets could be evaluated with the standard manual procedure and AERs were found. With the automated procedure only 19 of those data sets could be used for further comparisons. In the remaining 26 data sets no cluster, fulfilling all three selection criteria (plausibility in relation to head position, no scattering and no strong overlap with leftover heart activity), could be detected. Nevertheless, when comparing the 19 evaluable data sets, no significant difference between both methods could be detected. Both methods show an increase from baseline to the WOI, whereas neither baseline nor WOI were different. AER peaks were detectable in the signals of both selected clusters and neither their timing nor their amplitudes were significantly different. This is a surprising result as we saw, that the cluster selected by both methods were located rather far apart. One possibility for this distance, could be the dipolar signal pattern, another possibility the signal redistribution that happens during preprocessing [17]. These comparisons show, that the automated brain signal detection via PCA results in signals that are very similar to the signals obtained by manual evaluation and both of them can be used as brain signals for further comparisons. Even if only a fraction of the included data sets could be evaluated in the automated way, it is still a useful tool, since reproducibility of results is of importance. Additionally, the manual evaluation is optimized for peak detection, therefore its use is not applicable, if other aspects of the data need to be evaluated. In these cases, the PCA approach presents a possibility to select brain signals in a data driven way.

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