Comparing resting state fMRI cleaning approaches using multi- and single-echo acquisitions in healthy controls and patients with ADHD

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TARGET AUDIENCE: Researchers and clinicians interested in resting state fMRI, artifact removal and application in Attention Deficit Hyperactivity Disorder.

PURPOSE: Resting state functional MRI (rfMRI) is a powerful method for the investigation of brain functional connectivity and functional alterations caused by neurological diseases. Artifact removal is an intrinsic challenge of rfMRI data, since images are acquired without experimental modulation of brain function, thus with no a-priori knowledge about the signal of interest. It has been shown that even small head movements (≤1mm) can lead to spurious functional connectivity among anatomically distant areas[1,2]. Several methods for artifact removal have been developed, mainly based on the estimation and regression against potential sources of bias, such as motion parameters, white matter and cerebro-spinal fluid signals. An ICA-based artifact removal procedure, namely FMRIB's ICA-based X-noiseifier[3] (FIX), which uses an ICA component classifier for the automatic classification of good and bad components, has shown great ability to detect artifactual components and 'clean' single echo (SE) echo-planar imaging (EPI) data. Another proposal involves the combination of multi-echo (ME) EPI and ICA - MEICA[4,5]. This is an automatic cleaning method able to distinguish BOLD and non-BOLD components by means of the linear TE dependence of BOLD signal. This preliminary study aimed at comparing the above data-driven cleaning procedures on data from healthy controls (HC) and Attention deficit hyperactivity disorder (ADHD) patients. We qualitatively show the ability of the different methods to remove artifacts from a dataset that includes both typical subjects and subjects with a neuropsychiatric disorder, characterised by restlessness and high degree of head movements.

METHODS: For this preliminary study, we used a sample of 10 HC (34.1±10.7yrs, M/F: 7/3) and 10 age-matched ADHD patients (34.1±8.8yrs, M/F: 6/4). Resting state images were acquired using a 1.5T Siemens scanner with an ME EPI sequence[6] (TR=2570 ms; TE= 15, 34, 54 ms; resolution=3.75×3.75×4.49 mm; 31 axial slices; 200 volumes). ME EPI images were preprocessed with AFNI[7] (preprocessing steps included despiking, slice time correction, motion and anatomical co-registration parameters estimation, ME time courses combination with a T_2^* weighting scheme) and cleaned with the AFNI tool *meica.py* (MEICA approach). Images obtained with TE=54s were also used as single-echo EPI scans and were preprocessed with FSL (preprocessing steps included motion parameters estimation, brain extraction, spatial smoothing and high-pass temporal filtering). The outcome, called SE-Uncleaned approach from now on, was cleaned with 3 different data-driven cleaning approaches: regression of motion parameters, mean white matter signal and mean cerebrospinal fluid signal (MWC approach), FIX cleanup with soft (FIXsoft approach) and aggressive (FIXagg approach) cleaning options[8]. For explorative purposes, the weighted mean of the 3 echoes in the ME dataset, optimally combined to give the best T_2^* contrast[4], were also preprocessed with AFNI, then high-pass temporal filtered with FSL to compare the SE-Uncleaned images with the MEICA ones (ME-Uncleaned approach). The cleaning procedures were first compared in terms of temporal signal to noise ratio (tSNR): i.e., the group-averaged ratio between the mean and the standard deviation of each brain voxel across time. Spatial group-ICA was performed for each cleaned dataset after concatenating in time HC and ADHD groups, in order to compare the number of resting state networks (RSNs) extracted and their quality in terms of signal focused within the cortical areas. From the cleaned datasets, we also extracted subject-specific RSNs with template-based dual regression[9] using ten RSNs[10] as common spatial regressors. We then used the subject-specific RSN time series to estimate the mean power spectra of each cleaned dataset. It was obtained by scaling the cleaned time series of each RSN for the standard deviation of the corresponding SE-Uncleaned time series, averaging the spectra across the 20 subjects and calculating the median across the RSNs.

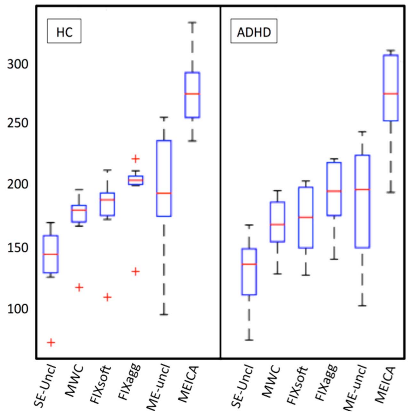

Fig.1. Temporal SNR estimation for various cleaning procedures.

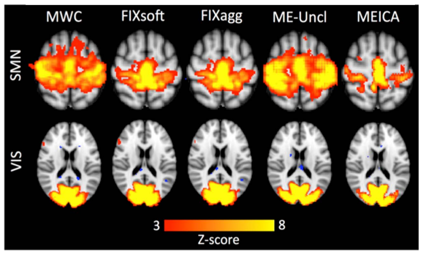

Fig.2. SMN and VIS extracted from each cleaned dataset, obtained by concatenating HC and ADHD and performing spatial group-ICA.

RESULTS: Fig.1 shows the tSNR for each cleaning procedure. ME-Uncleaned and MEICA tSNRs were scaled dividing by the square root of 3 to adjust for the different number of images per time point. As expected, the SE-Uncleaned tSNR was significantly lower ($p<0.01$) than the cleaned and ME-Uncleaned ones. As regards the HC group, all the comparisons between tSNR pairs highlighted strongly significant differences, except for the FIXagg - ME-Uncleaned pair. MEICA tSNR was significantly higher ($p<0.001$) than the others in both the groups. However, in the ADHD group, we did not found significant differences between the tSNR of the SE cleaned datasets and the ME-Uncleaned tSNR, probably due to the large standard deviation in the pathological group. Fig.2 shows two typical RSNs, the Sensory Motor Network (SMN) and the Visual Network (VIS), extracted from each dataset by means of the group-ICA. Interestingly, in MEICA RSNs the activation areas are well focused into the cortical areas, while the RSNs obtained with the other cleaning procedures are more blurred. Moreover, from the 25 components extracted from each dataset, only 14 were recognized as BOLD components among the MWC and ME-Uncleaned ones, while 17 good components were recognized from FIXsoft, FIXagg e MEICA group maps. Fig.3 shows the power spectra obtained for all the cleaned datasets. MWC and FIXsoft spectra showed the highest power at high frequencies (non-BOLD signal). FIXagg spectra showed a power reduction both at low (BOLD signal) and at high frequencies, while MEICA performed a good reduction of the non-BOLD frequencies, although it requires acquisitions not generally available on clinical scanners.

DISCUSSION: tSNR, estimated from the SE cleaning approaches, highlighted the ability of FIX in reducing signal fluctuations in healthy subjects, but not in ADHD patients, probably due to greater extent of head movements in the latter group. However, it is noteworthy that MEICA approach preserved high tSNR values even for the pathological dataset. Group-ICA provided qualitative information on the ability to extract common spatial patterns from a small dataset of 20 subjects. Group-ICA performed on FIX and MEICA datasets returned a higher number of "good" components, showing a better ability in removing artifactual components in the cleaning steps. This result indicates that these cleaning methods allow a more detailed analysis of network connectivity by providing more good components as group-ICA outcome. Moreover, RSNs obtained from these three datasets show more focal signal, which means a good performance of the cleaning procedure. The blurring contours in the FIX RSNs could probably be due to the spatial smoothing performed as preprocessing step on the SE datasets, which can be avoided with MEICA. Indeed, the sharp shape of the MEICA RSNs is noteworthy, especially considering the small data sample. Power spectra results suggest that MEICA is probably the cleaning method which best reduces high frequencies related to motion and physiological noise.

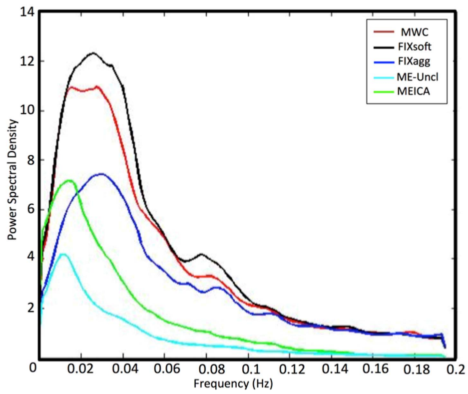

Fig.3. Temporal power spectra for different cleaning approaches, averaged across subjects and calculated median across components.

CONCLUSION: This preliminary study highlighted better performances of the MEICA approach for artifact removal compared to other standard cleaning procedures. However, other analyses need to be done to evaluate MEICA's efficacy in preserving inter-group variability of interest and detecting functional connectivity differences in ADHD patients compared to HC.

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