How the cleaning of resting state fMRI data affects the detection of functional connectivity alterations in Alzheimer's disease

Ludovica Griffanti[1,2], Ottavia Dipasquale[1,2], Maria Marcella Laganà[1], Raffaello Nemni[1,3], Mario Clerici[1,3], Stephen Smith[4], Giuseppe Baselli[2], and Francesca Baglio[1]

[1]IRCCS, Fondazione don Carlo Gnocchi, Milano, Milan, Italy, [2]Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy, [3]Physiopatholgy Department, Università degli Studi di Milano, Milan, Italy, [4]FMRIB (Centre for Functional MRI of the Brain), Oxford University, Oxford, United Kingdom

Target audience: Researchers and clinicians interested in resting state fMRI, artefact removal, and application in aging and dementia.

Purpose: Resting state functional MRI (rfMRI) is a widespread technique for investigating brain functional connectivity (FC) in both healthy and diseased populations. In Alzheimer's disease (AD) patients, decreased FC is usually observed in the posterior cingulate cortex (PCC) within the default mode network (DMN), and this is becoming a possible biomarker for AD. However, the presence of artefacts in the data represents a challenge for the correct identification of resting state networks (RSNs) and the evaluation of their connectivity, especially in presence of pathological alterations (e.g., atrophy). There is growing interest in the development of cleaning procedures, especially those not requiring external recordings (data-driven) and which are able to remove multiple sources of artefacts. It is important that only inter-subject variability due to the artefacts is removed, preserving the ability to capture between-subject variability of interest - crucial in clinical applications to discriminate different pathologies and monitor their staging. The aim of this study was to compare different data-driven cleaning procedures on data from elderly healthy subjects and AD patients in a mild or moderate stage of the disease, and to evaluate their impact on the ability to detect the typical DMN alteration in AD.

Method: rfMRI data from 21 AD patients (73.62±5.22 yrs, M/F:8/13) and 20 age-matched healthy controls (HC, 71.05±3.66 yrs, M/F:7/13) were acquired using a 1.5T Siemens scanner (TR/TE=2500/30 ms; resolution=3.1x3.1x2.5mm; 39 axial slices; 160volumes). After standard preprocessing with FSL, we compared different data-driven cleaning approaches: regression of 24 motion parameters (MOTreg); regression of motion parameters, mean white matter signal and mean cerebrospinal fluid signal (MWCreg); FMRIB's ICA-based X-noiseifier (FIX)[1] cleanup with soft (FIXsoft) and aggressive (FIXagg) cleaning options[2]. The cleaning procedures were firstly compared in both groups in terms of BOLD signal fluctuation reductions with respect to the uncleaned data[3]. For each subject we calculated $\%\Delta STD_{map}=(STD(img_{uncl})-STD(img_{clean}))/STD(img_{uncl})*100$, where $STD(img_x)$ is the temporal standard deviation of image x. These images were then used to build, for each group, a probability map of areas where $\%\Delta STD_{map}>25\%$ across subjects. With the cleaned datasets obtained with the different options, we then performed a FC analysis of the DMN with template-based dual regression[3] using ten major RSNs[4] as common spatial regressors. Finally, we compared the FC results in terms of within-group consistency (standard deviation across subjects) and of ability to identify FC alterations in AD patients (two sample t-test, $p<0.05$, corrected for multiple comparisons after initial cluster-forming thresholding at $p_{uncorr}<0.05$).

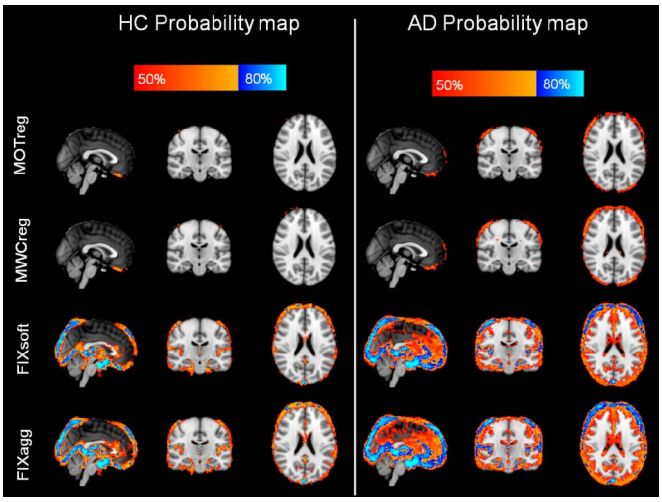

Fig.1. Spatial pattern of change in BOLD signal standard deviation: probability map of arease where $\%\Delta STD>25\%$ across all subjects.

Results: Fig.1 shows the probability maps of BOLD fluctuation reduction across subjects in the two groups: the reduction is localized at brain boundaries after MOTreg, a small further decrease involves the ventricles and the WM after MWCreg, a big reduction within ventricles, but also involving areas corresponding to blood vessels can be observed after FIX cleanup. Regarding FC analyses, in both groups the consistency increased after cleaning (lower standard deviation across subjects, Fig.2). The highest consistency was achieved with MWCreg and FIXagg. The consistency was, in general, higher within the HC group than in the AD group. Fig.3 shows the between-group differences in template-based dual regression for each cleaning procedure. A significant FC decrease in the AD group was observed only after both FIXsoft and FIXagg cleanup (FIXagg>FIXsoft), in precuneus, PCC, bilateral inferior parietal lobule, right fusiform gyrus, and right parahyppocampal gyrus.

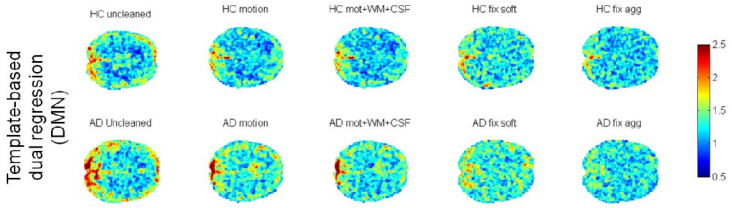

Fig.2. Within-group consistency (standard deviation of z maps across subjects) of DMN FC analysis after various cleaning procedures.

Discussion: The spatial pattern of BOLD fluctuation reduction is in line with the spatial characteristics of the removed artefacts and suggests that FIX is able to identify and remove physiological noise (vascular and CSF pulsation artefacts) without needing external recordings. The FC results demonstrate that a measure of within-group consistency is not necessarily sufficient as a reliable measure of effectiveness of a cleaning procedure, because it is possible that useful across-subject variability is removed with the cleaning or that the cleaning is not effective enough to capture the between-group differences. Among the tested approaches the best results were obtained with FIX, which is the only method that allowed detecting of the expected DMN FC alteration in AD, even in mild to moderate stages of the pathology. The results were more significant with FIXagg. This option seems to be more effective on data from elderly healthy subjects and patients, acquired with a clinical scanner, while the use of FIXsoft is recommended on data with higher spatial and temporal resolution and healthy subjects.

Conclusion: We have demonstrated the importance of an effective cleaning of rfMRI data for sensitive detection of FC alterations, for example those observed in AD.

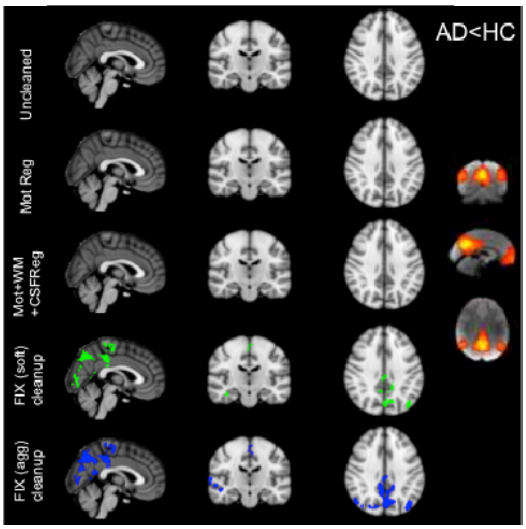

Fig.3. Results of template-based dual regression (the DMN template map is shown on the right). Significantly decreased FC within the DMN in the AD group was detectable only after FIX cleanup.

References:

[1]Salimi-Khorshidi G, Douaud G, Beckmann C, et al. Automatic Denoising of Functional MRI Data: Combining Independent Component Analysis and Hierarchical Fusion of Classifiers (under review);

[2]Griffanti L, Salimi-Khorshidi G, Beckmann C, et al. Improving resting state fMRI data quality through accelerated acquisition and automatic denoising, OHBM 2013;

[3]Khalili-Mahani N, Chang C, van Osch MJ, et al. The impact of "physiological correction" on functional connectivity analysis of pharmacological resting state fMRI. NeuroImage 2013; 65:499-510;

[4]Smith S, Fox P, Miller K, et al. Correspondence of the brain's functional architecture during activation and rest. PNAS 2009; 106(31):13040-45.