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Evaluation of the MCFLIRT Correction Algorithm in Head Motion from Resting State fMRI Data

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***Abstract*—**In the last few years, resting-state functional MRI (rs-fMRI) was widely used to investigate the architecture of brain networks by investigating the Blood Oxygenation Level Dependent response. This technique represented an interesting, robust and reliable approach to compare pathologic and healthy subjects in order to investigate neurodegenerative diseases evolution. On the other hand, the elaboration of rs-fMRI data resulted to be very prone to noise due to confounding factors especially the head motion. Head motion has long been known to be a source of artefacts in task-based functional MRI studies, but it has become a particularly challenging problem in recent studies using rs-fMRI. The aim of this work was to evaluate in MS patients a well-known motion correction algorithm from the FMRIB's Software Library - MCFLIRT - that could be applied to minimize the head motion distortions, allowing to correctly interpret rs-fMRI results.

***Keywords*—**Head motion correction, MCFLIRT algorithm, multiple sclerosis, resting state fMRI

I. INTRODUCTION

IN the recent years, functional MRI (fMRI) became important in scientific field since it is a particular MRI sequence that represents a measure of brain activity detecting cerebral changes associated with blood flow. For this goal, several studies based on the functional MRI (fMRI) were developed in order to explore the architecture of brain networks and their interaction [1]-[4]. The aim of these studies was to extract clinically useful and novel knowledge from neuroimaging data. Resting state fMRI (rs-fMRI) is a particular type of fMRI, focused on the activation of specific brain networks in rest condition and on how they interact with each other. It represents an innovative technique to understand cerebral mechanism behind brain networks interactions. But this kind of data is very complex, and its elaboration is difficult especially for the presence of noise and interferences derived by several sources. These sources can be external, i.e. network interference, or internal, i.e. involuntary muscle movements of the patient.

Usually, the external causes are minimized using the right wires or other physical precautions, while internal ones can represent issues leading to BOLD signal distortion. In particular, in this field, head motion has become a particularly challenging problem using fMRI [4]. In fact, head motion during fMRI scanning provokes misalignment of one volume to the next, introducing measurement inaccuracies as imaging voxels does not represent identical brain regions over time [5]. It is essential to check and to correct these motion effects between volumes over the course of the fMRI experiment [6]. Motion correction is the operation in which happens the estimation of the body movement parameters and their application into motion transforms to realign the time series of brain images. Usually, software for the fMRI data elaboration have an algorithm for the motion correction. Application of these algorithms has the purpose of minimizing distortions derived by the movements, allowing the data processing. One of the most used is MCFLIRT [7] algorithm, which is implemented in FMRIB's Software Library (FSL) [8].

MCFLIRT is an intra-modal motion correction tool designed for use on fMRI time series and based on optimization and registration techniques. It loads the time-series in its entirety and the middle volume represents the initial template image. A coarse 8-mm search for the motion parameters is then carried out using the cost function specified followed by two subsequent searches at 4 mm using increasingly tighter tolerances. All optimizations use trilinear interpolation. In the second phase, an identity transformation is assumed between the middle volume and the adjacent volume. The transformation found in this first search is then used as the estimate for the transformation between the middle volume and the volume beyond the adjacent one. This pattern should lead to much faster optimization and greater accuracy for the majority of studies where subject motion is minimal. In the pathological cases, this scheme does not penalise the quality of the final correction.

The aim of this work was to evaluate the ability of MCFLIRT motion correction in Multiple Sclerosis (MS) patients in order to verify its effectiveness into minimizing the head motion distortions, allowing to correctly interpret rs-fMRI results. For this goal, we have considered the head as a rigid body. Thus, head position is described at each timepoint by six parameters: translational displacements along X, Y, and Z axes and rotational displacements along phi (roll), theta (pitch) and psi (yaw) axes.

Using these parameters, we performed an analysis of the movements considering each subject and not only the whole group. Each motion characteristic was compared with a limited condition in order to investigate possible outliers, which could invalidate the analysis.

II. MATERIALS AND METHODS

A. Subjects

18 consecutive patients with relapsing-remitting MS within two years of disease presentation (early-MS; mean-age 37.42±8.11, nine females) were enrolled according to revised McDonald criteria [9], and matched for demographic variables

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with 19 healthy controls (mean-age 37.55±14.76, 10 females). All subjects were recruited from the Neurological Unit of the University 'Magna Graecia' of Catanzaro.

The MS patients met the following criteria: (1) no history of traumatic brain injury, past or current history of substance abuse, or other coexisting medical conditions; (2) no clinical relapses for at least three months prior to study entry; (3) no assumption of steroids, or disease-modifying therapies in the three months before recruitment. Inclusion criteria for healthy subjects were: (1) no previous history of neurological or psychiatric diseases; (2) normal MRI of the brain (as assessed by structural MRI scanning) and (3) no assumption of drugs acting on the central nervous system.

All participants provided written informed consent and the study was approved by the local institutional review board.

B. MRI Acquisition and Elaboration

MRI were acquired by a 3T scanner with eight channel head coils (Discovery MR-750, GE, Milwaukee, WI, USA), including: (a) whole-brain T1-weighted (SPGR; TE/TR=3.7/ 9.2 ms, flip angle 12°, voxel-size 1×1×1 mm^3); (b) conventional T2-weighted; (c) resting-state functional MRI (rs-FMRI), 200 volumes of a repeated gradient-echo echo planar imaging sequence (TR/TE: 2000/25 msec; thickness/ gap=3/0.8 mm).

Sequences of rs-fMRI were pre-elaborated with tools restrained into FSL software v.5.0. Each of these has been submitted the same pre-processing steps, which provided five important points: (i) elimination of first five volumes; (ii) bet extraction; (iii) calculation of motion parameters for the distortion correction; (iv) application of a high pass filter (128s) and (v) elaboration of a Gaussian kernel (8 mm) for image smoothing.

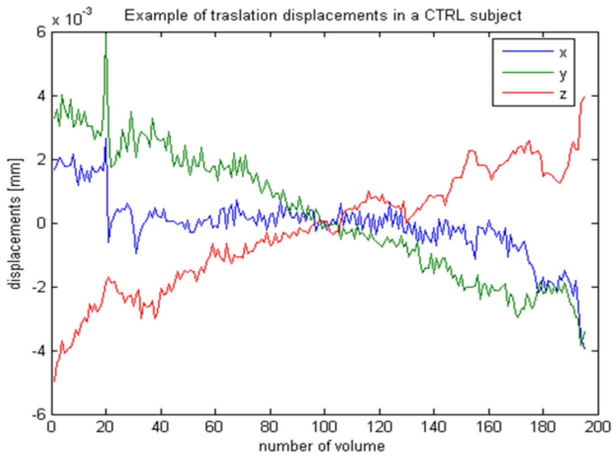

Fig. 1 Translational movements obtained considering a control subject

After, they were motion corrected through MCFLIRT [7] algorithm for extracting the six motion parameters: three translation measures of axes X (left/right), Y (anterior/ posterior) and Z (superior/inferior) and three rotations measures around the axes phi (roll), theta (pitch) and psi (yaw).

To characterize head movements for each subject, two estimations derived from the three translational and rotational displacements have been calculated. In particular, we computed the root-mean-square (RMS) from the X, Y and Z parameters, while we calculated the Euler-Angle (EA) from phi, theta, and psi angles. Moreover, for each subject, the means of each previous variable have been computed, in order to create a complete characterization. In addition, to evaluate data dispersion, also deviation standard (std) for the three translational and rotational displacements have been obtained.

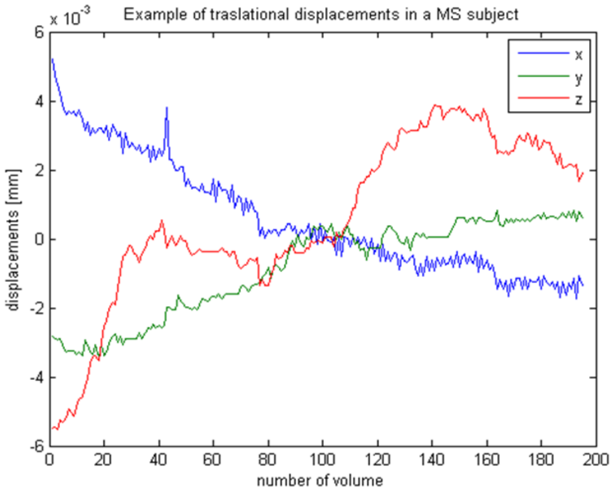

Fig. 2 Translational movements obtained considering a Multiple Scleroris subject

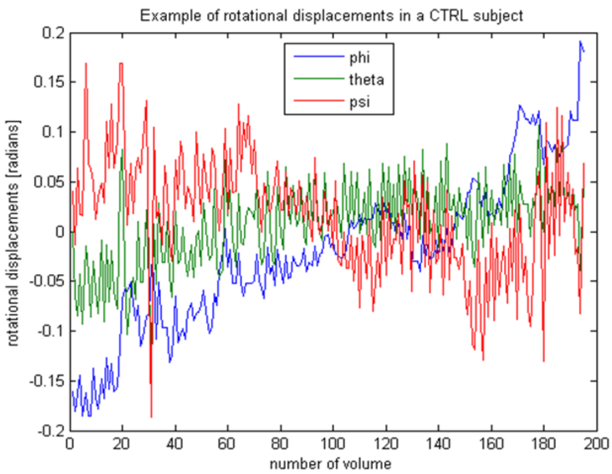

Fig. 3 Rotational movements obtained considering a control subject

C. Outlier Analysis

We performed an outlier analysis comparing each subject's RMS/EA with the sum of its group mean and two standard deviations. This represented our limited condition, and we defined it as S (rms), for the translations and S (EA) for the rotations given in (1) and (2).

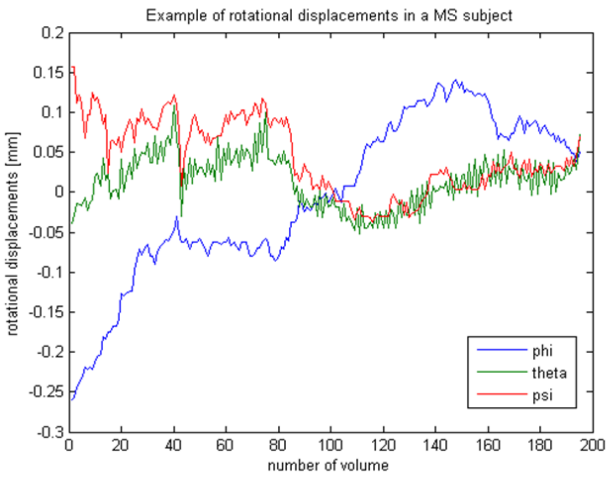

Fig. 4 Rotational movements obtained considering a Multiple Sclerosis subject

$$S\ (rms) = mean\ rms\ group + 2 * std\ rms\ group \quad (1)$$

or

$$S\ (EA) = mean\ EA\ group + 2 * std\ EA\ group \quad (2)$$

in which *mean rms/EA group* represented the mean of rms/EA within the two groups (MS and CTRL), *std rms/EA group* was the standard deviation calculated in the groups, and *S rms/EA* was the outlier condition for rms/EA.

We classified a subject as outlier if its value exceeded this sum, and its movement could distort the fMRI analysis.

We performed two different analysis: (i) considering each single subject, rms and EA values have been compared with the limited condition; (ii) considering the entire groups, a t test has been carried in order to evaluate any differences into movements between the two groups.

III. Results

Analysis showed two outliers in healthy-control (EA= 2.8819, S=2.73; RMS=0.0083, S=0.0061) and in MS-patients (EA=2.9532, S=2.7951; RMS=0.022, S=0.0137). These results for both groups are reported in Tables I and II. Moreover, a t-test was realized to investigate the differences between the two groups. No statistical significant differences ($p<0.05$) were found in RMS values (MS-mean = 0.0040 mm and healthy-mean = 0.0026 mm) and in EA (MS-mean = 1.7201° and healthy-mean = 1.5731°).

TABLE I
Parameters of Outlier Analysis in CTRL Group

Displacement	Estimator	Outlier form	Outlier value	Any outlier
Translational [mm]	Root mean squared - rms	Rms + 2*std rms	0.0061	*0.0083*
Rotational [grades]	Euler Angle	EA + 2*std EA	2.73	*2.88*

TABLE II
Parameters of Outlier Analysis in MS Group

Displacement	Estimator	Outlier form	Outlier value	Any outlier
Translational [mm]	Root mean squared - rms	Rms + 2*std rms	0.0137	*0.022*
Rotational [grades]	Euler Angle	EA + 2*std EA	2.7951	*2.9532*

IV. Discussion

We analyzed movements derived from head motions in MS patients to respect healthy controls in order to evaluate the correction performance of MCFLIRT algorithm. We demonstrated in this study that this approach was able to correct the head motion considering all subjects and all groups, but it was less effective in the single subject analysis. These findings represent interesting and important evidences in the rs-fMRI elaboration. In fact, head motion significantly affects the measures of functional connectivity MRI, in particular in studies where the aim is to compare groups that differ in their tendency to move. These will be particularly vulnerable to the confounding effects of motion [4].

In this study, we effectuated two different analysis considering the entire group and the single subject, in which we found two outliers in both controls and MS groups.

The considered movements were translational (along the axes X, Y and Z) or rotational (respect the angle phi, theta and psi). We calculated two estimators to describe the two different kinds of motion: (i) root-mean-squared (rms), to investigate the translational displacements; (ii) Euler Angle (EA), for the rotations.

The mean value of rms and EA has been calculated for each subject and for both groups. The limited conditions are reported previously in (1) and (2).

When we performed the analysis considering each single subject, interestingly we found two outliers in both groups (see Tables I and II). This result was in contrast with the analysis considering the two entire groups, since t-test showed a non-significant result between the groups' movements. These results provide new insights about this motion correction algorithm, which could have practical implications, due to incorrect adjustment of the volume alignment into image scanning. Moreover, MS subjects presented major values in head motions respect the healthy controls. It could depend on the pathology, and for this reason, it could be more complicated for the algorithm to minimize the distortions.

In our study, pathological subjects were affected by early MS, and the stage of disease was initial. Therefore, the outlier found showed not high deviations from the limit condition, but their presence could be a problem for the analysis. Moreover, probably with the disease evolution towards more serious conditions, these values could increase, resulting in a decrease in the noise signal ratio. Analysis in this condition is more complicated, and the final results could be incorrect.

A clear implication of the present results is that it will be desirable to carefully consider the effects of head motion on functional MRI studies, examining individual signals rather than entire groups' differences. Therefore, we suggest that there is the necessity to implement a further protocol to improve the denoising operation. A first step could be to study different pathologies and define the principal movements for each of these. The aim is to characterize each disease with ad hoc protocol, in order to accelerate and to obtain better analysis.

V. Conclusion

Head motion has significant effects on rs-fMRI network measures and it is usually associated with uncorrected changes in functional connectivity of brain networks. Strategies to reduce this distortion are fundamental for a correct data interpretation. We analyzed one of the most used motion correction algorithms, MCFLIRT, and our evaluation showed that it is able, in early MS patients to respect healthy controls, in order to minimize effects of head motions, correcting any movements' artefacts considering the entire groups. But, the application of this algorithm considering each subject could not be effective to minimize the distortions. In fact, we found two outlier subjects in both groups in our movements analysis.

An interesting step to overcome this drawback could be represented by a characterizing of the movements basis on the considered pathology. In this manner, ad hoc protocol could be realized in order to minimize the distortions derived by the major movements interested in the pathology. In future works, we planned to evaluate the most important head motion in MS patients to respect healthy controls in fMRI sequence, in order to make first step into a personalized future strategy for the motion correction. This finding could be an important step into characterizing fMRI study in MS, focusing on the strategies to minimize this movement, e.g. using particular bare sit or the right filter into pre-processing step.

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