SyN based multimodal investigation on a small cohort of patients affected with Amnesic Mild Cognitive Impairment

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INTRODUCTION In the last years the MRI computational anatomy is increasingly taking advantage of new promising deformable mapping techniques. Particularly encouraging results were obtained by the Symmetric Normalization (SyN) method, developed by Braian Avants and his co-workers (1). SyN comes out to be the more accurate registration method out of 14 registration methods compared, as reported in a recent paper (2). It is well known that the use of a good registration method is the basis of a morphometric investigation (3,4). In a multimodal investigation the normalization algorithm is even more important, as the intra-subject inter-modality variability, beside the inter-subject variability, has to be taken into account. There is evidence that gray matter atrophy and iron content in the brain are related not only to normal aging (5), but also to various pathological conditions as Parkinson, Alzheimer Disease, Levy Body Dementia (6) and Multiple Sclerosis as recently found (7). To the best of our knowledge studies reporting differences in iron content in Mild Cognitive Impairment are absent in literature, and GM atrophy patterns were not assessed in a-MCI except for limited regions, where they have been assumed as predictors of the risk of conversion (8). We assessed the SyN effectiveness to address multimodal investigations in the early stages of the disease. We used SyN, according to its implementation in the ANTs software repository, to assess for differences between a group of 10 subjects affected by Amnesic Mild Cognitive Impairment (a-MCI) and a group of 10 control subjects (matched for age and sex). In particular our multimodal investigation consisted in GM morphometry combined with GM transverse relaxometry (for the iron content evaluation). **MATERIAL AND METHODS** Twenty subjects, 10 patients affected by a-MCI and 10 control subjects underwent the investigation. The MRI protocol was performed on a GE MR750 3T scanner, equipped with an 8 channel RX Head Coil. The Protocol consisted in a T1 weighted high resolution image, an SE and a GE segmented EPI both acquired twice with a low TE (12.9ms and 6.7ms respectively) and 4 times with an higher TE (32ms and 81ms respectively). The EPI acquisitions were used to extract the relaxometry maps R2 ,R2s and R2'. The statistical analysis was performed through non parametric permutation statistics (9). All the post-processing was implemented on a Mac Pro 8-core 1.64MHz computer by using ANTs, Matlab and FSL software (the procedure is depicted in Fig.1). **RESULTS AND CONCLUSIONS** The morphometric investigation revealed differences in the right hippocampus and medial parahippocampal gyrus, and in the anterior part of the parahippocampal and fusiform gyrus bilaterally (Fig.2). Due to the small cohort of patients, probably, our results did not exhibit significance at the cluster level. The relaxometry analysis (R2, R2* and R2', see Fig.3) didn't show any difference in the two groups, neither in a voxel based approach nor in the analysis performed on 90 selected GM areas (AAL atlas labels, SyN registered to our template, Fig.4). The absence of abnormal iron accumulation evidence, might, in principle, suggest the lack of sensitivity of the technique (on such a limited sample), but might also be due to the affective absence of abnormal iron concentration in the early stage of the disease (as suggested by the accurate overlapping of the red and blue curves from the region based analysis, in Fig.4).

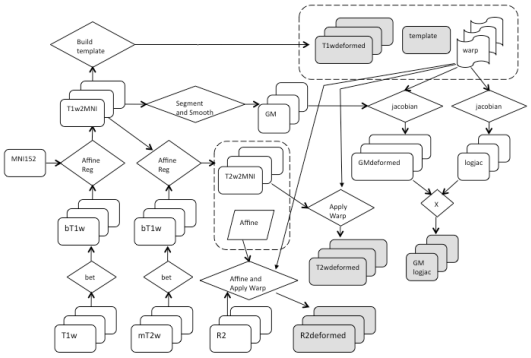
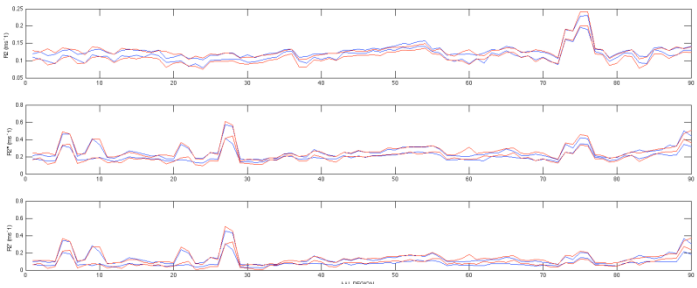


Figure 1. The procedure adopted in the present study. The R2 images (same for R2*) are obtained by the 6 T2 (T2*) weighted ones, realigned and fitted to a mono-exponential dacay model. R2' is obtained as the difference between R2* and R2.

Figure 4. The mean+stdev and the mean-stdev among subjetcs were plotted across 90 AAL regions for R2, R2* and R2' (control group blue, patients group red).



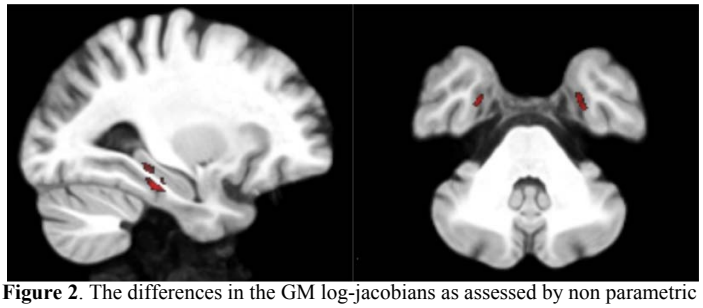


Figure 2. The differences in the GM log-jacobians as assessed by non parametric permutation statistics are superimposed to the template (see text). The Z value at the cluster corrected level is show (but it is below the 0.95 confidence interval)

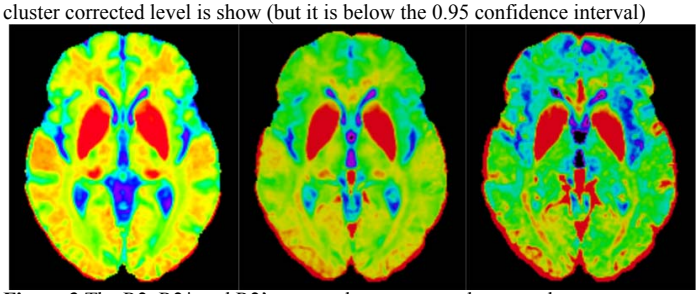


Figure 3 The R2, R2* and R2' mean values maps on the control group.

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