Comparison of Corpus Callosum Area and whole Brain Volume as markers of brain atrophy in Multiple Sclerosis

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INTRODUCTION

Measures of brain volume (BV) loss are currently used as valid methods for evaluating atrophy in MS clinical trials alongside MRI measures of disease activity. However, the currently available methods for measuring brain atrophy based on BV show poor sensitivity and high variability both among and within individuals, which lead to differences in outcome that apply to clinical trials, and prevents their use for the evaluation of brain atrophy at individual level. Measures of corpus callosum (CC) have been proposed as alternative markers of brain atrophy, but their effectiveness and relation with BV still need to be defined. The purpose of this study is to compare the intra-individual variations of normal brain volume (BV) with corpus callosum area (CCA) as markers of brain atrophy in MS, to assess their correlation with clinical parameters and to evaluate their relative effectiveness as outcome measures for clinical trials.

METHODS

Patients (n=40) were selected from those attending the local Multiple Sclerosis Regional Center of the Careggi University Hospital. Inclusion and exclusion criteria: a) diagnosis of MS (McDonald 2010); b) relapsing-remitting (RR) course; c) availability of a MR scan within the first year from the diagnosis; and d) no evidence of CNS comorbidity beside MS; e) age, 18-55. To take into account the fact that some patients progressed several points in the EDSS scale during the period of observation, but that a difference in the EDSS score of two steps can be considered a strong indicator of clinical change, the change in EDSS was categorized with the following score: 1, for patients who did not progress during the period of observation; 2, for patients who progressed up to two steps (1 point) in the EDSS scale between 0 and 5.0 (and one step above 5.5); 3, for each further whole step of point progression in the scale.

RESULTS

The demographic, clinical and MRI characteristics of the patients at baseline are summarized in Table 1. The results of the measurements of CCA and of NBV are summarized in table 2 and fig. 1A and 1B. Correlation between t1 and t2 was high for CCA and low for NBV (Table 3; fig. 1C and 1D). Absolute and percentage change mean of CCA and of NBV within 5 years is reported in Table 3; the percent change of CCA was greater than NBV change (p<0.05). Association of CCA and of NBV with a number of clinical and demographic variables was tested with a multivariate analysis. Greater disability progression and an high lesion load were associated with increased odds (respectively 3.34; 95%CI 0.64-19.39; 1.24; 95%CI 1.1; 1.48) of a greater percent variation of CC area, but not of BV (Table 4). Using these data, power comparison of the two biomarker as outcome measures in clinical trials was carried out, indicating that using CCA would yield approximately a 50% reduction of the sample size required in longitudinal re-

CONCLUSIONS

A wider intra-individual variability of NBV compared with CCA is indicated by the smaller internal correlation coefficient between the values obtained in the t1 and t2 MRIs. Among the factors that may account for the wider intra-individual variability of BV there are biological factors, technical factors and factors related to the software used for the postprocessing. The results in our sample suggest that the factors that affect brain volume may have less impact on CCA. In conclusion, CC area seems more sensitive and reliable than BV as an atrophy marker. CC area change over time also seem more closely associated to disability changes. CCA could therefore be used as a biomarker in clinical MS practice as well as in clinical trials investigating atrophy, providing greater reliability at the intra-individual level and lowering sample size required in longitudinal re-

REFERENCES