Corpus Callosum Atrophy Rate in Mild Cognitive Impairment and Prodromal Alzheimer's Disease

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TARGET AUDIENCE:

Researchers interested in neuroimaging biomarkers of Alzheimer's disease (AD) progression.

PURPOSE:

Corpus callosum (CC) size and shape have been previously studied in Alzheimer's disease (AD) with the majority of studies having been cross-sectional. Due to the large variance in normal CC morphology, cross-sectional studies are limited in statistical power, calling for longitudinal data to determine individual rates of change. Physiological changes are particularly relevant in mild cognitive impairment (MCI), in which CC morphology has not been previously studied longitudinally. We examined temporal rates of change in CC morphology in MCI patients over a one-year period, and determined whether these rates differ between MCI subjects who convert to AD (MCI-C) and those who do not (MCI-NC).

METHODS:

Subjects: We used 138 MCI subjects' scans from Alzheimer's Disease Neuroimaging Initiative (ADNI) database[1] where 81 (51 males/30 females) converted to AD with a mean (±SD) baseline-to-conversion time of 2.3 (±1.4) years and 57 (46 males/11 females) remained as MCI over the mean (±SD) observation period of 5.4 (±1.6) years. Imaging: Scans consisted of 1.5T, T1-weighted MP-RAGE images with matrix sizes of 192×192×160-170 or 256×256×166-184, in-plane voxel size = 0.94-1.25mm, slice thickness = 1.2mm. Measurements: A novel multi-atlas based algorithm -Automatic Registration Toolbox (ART) module 'yuki'- was used to automatically segment the mid-sagittal cross-sectional area of the CC and measure the total area (CCA), circumference (CCP), and five sub-regional areas. Circularity (CIR) - a measure of CC shape - was defined as $4\pi \times CCA/CCP^2$. The percent baseline to follow-up rate of change per year (the annual percent change (APC)) of CIR, CCA and five sub-areas were compared between MCI-NC and MCI-C subjects. Statistical analysis: The CC measures were modeled as a linear function of age, education, sex, group (MCI-NC vs. MCI-C) and the sex-by-group interaction. In case of significant sex and group interaction, comparisons between the two groups followed for each sex, otherwise the model was refitted without the non-significant variable.

Table 1: APC (mean ± 95% confidence interval)

	MCI-NC	MCI-C
rCIR	**-0.89**±0.37	**-1.85**±0.31
†rCCA (F)	0.02±0.60	**-1.22**±0.36
†rCCA (M)	**-0.64**±0.29	**-0.75**±0.28
†rGenu/rostrum (F)	-0.02±1.20	**-2.03**±0.73
†rGenu/rostrum (M)	**-0.98**±0.59	**-1.23**±0.56
rAnterior-body	**-0.73**±0.63	**-0.59**±0.53
rMid-body	-0.43±0.62	0.09±0.52
rPosterior-body	-0.02±0.69	0.04±0.58
†rSplenium (F)	0.02±0.96	**-1.75**±0.58
†rSplenium (M)	-0.41±0.47	**-0.82**±0.44
†Group by sex interaction		

RESULTS:

The APCs and their 95% confidence intervals are given in Table 1 where rates that are significantly different from zero are shown in bold font. The CC became less circular (-0.89% per year in MCI-NC, -1.85% per year in MCI-C) over time, with faster decline in MCI-C (p=0.0002). In females, atrophy rates were higher in MCI-C relative to MCI-NC in total CC area (p=0.0006), genu/rostrum (p=0.005), and splenium (0.002). In males, these rates did not differ between groups.

DISCUSSION:

rCCA, rGenu/rostrum and rSplenium were significantly different only in the female MCI-C and MCI-NC subgroups, suggesting these abnormal rates would be predictor of future conversion to AD particularly in female MCI subjects. rCIR differentiated between MCI-C and MCI-NC subjects with the largest effect size (0.67), suggesting the temporal rate of change of CC circularity to be the most sensitive predictor of MCI to AD conversion. Comparison of the rCIRs to those reported in our pervious study[2] indicates CC in the MCI-NC group is aging normally while the changes in the CC morphology in the MCI-C group is at the level of very mild/mild AD. The spatial patterns of CC decline were also very similar to those obtained in our previous study[2] which mainly occur in the anterior and the posterior regions. Despite demonstrating comparable spatial patterns, HC/MCI-NC and AD/MCI-C groups are distinguished by the temporal rates of decline that are almost twice as fast in AD/MCI-C.

CONCLUSION:

We have shown that the spatial and temporal patterns of CC morphological change in MCI-NC are similar to HC, while those in MCI-C are similar to very mild/mild AD. We also verified that CC atrophy is quantifiable in a one-year longitudinal observation period, making this a practical imaging biomarker both for sample enrichment and as an outcome measure in clinical trials. Amongst the measures considered, circularity proved to be the most sensitive measure separating convertors from non-convertors regardless of their gender.

REFERENCES:

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