WHOLE BRAIN ATROPHY RATE IN RELATION TO COGNITIVE DECLINE IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT

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Introduction

Mild cognitive impairment (MCI) is considered to be an early stage of Alzheimer's disease (AD). Patients with AD and to a lesser extent MCI patients show brain atrophy on structural MRI. It has been suggested that rate of brain volume change over time is more sensitive to the earliest disease changes than brain volume measurements at a single time point.[1] [2] We determined the annual rate of atrophy in MCI and AD compared with controls. In addition, we looked at the correlation between (rate of) atrophy and (rate of) cognitive decline. Finally we compared the rates of atrophy between MCI patients who progressed to dementia and those whose diagnosis remained MCI.

Patients & Methods

We consecutively recruited 152 patients from our memory clinic. Sixty-eight patients were diagnosed with AD, 47 with MCI and 37 controls were included. Subjects underwent repeated MR imaging with an average scan interval of two years. The MMSE was used as a measure of general cognitive function. Annualized change in MMSE was calculated as a measure of cognitive decline. The baseline brain volume and annual rate of atrophy were calculated using the SIENA package (FSL: http://www.fmrib.ox.ac.uk/fsl/).[3] Analysis of variance and partial correlation were corrected for age and sex.

Results

Normalized brain volume at baseline was lowest for the AD group (mean ± SD 1449 ± 92mL) compared to MCI (1493 ± 78mL) and controls (1533 ± 87mL) (AD < MCI = controls; $p<0.001$, age and sex corrected) [fig1]. Differences between groups were more pronounced for whole brain rate of atrophy: the AD group (-1.9 %/y ± 0.9) had a higher rate of atrophy than the MCI group (-1.2 %/y ± 0.9) who on their turn had higher rates of atrophy than the control group (-0.6 %/y ± 0.6) (AD < MCI < control; $p<0.001$, age and sex corrected) [fig2]. Across diagnostic groups, baseline brain volume and the rate of brain atrophy correlated with baseline MMSE ($r=0.32$, $p<0.001$ and $r=0.47$ $p<0.001$, respectively), while only rate of atrophy correlated with annualized MMSE change ($r=0.47$ $p<0.001$) [fig3]. Of the 47 patients diagnosed with MCI at baseline, thirty-one patients progressed to dementia, and for 16 patients the diagnosis remained MCI. There was no difference between these groups with respect to baseline whole brain volume ($p= 0.12$ age/sex corrected), but whole brain rate of atrophy (-1.4%/y ± 1 vs -0.9%/y ± 0.6; $p=0.035$, $p=0.053$ age/sex corrected) was higher in the progressive MCI patients than in the stable MCI patients

Discussion / Conclusions

While baseline brain volume was lower for AD than MCI and controls, it did not discriminate MCI from controls. By contrast, whole brain rate of atrophy did differ significantly between all three groups: MCI patients had atrophy rates between AD and controls. The clinical relevance of these markers was demonstrated by the correlation of baseline brain volume with baseline cognition and rate of atrophy with baseline cognition and cognitive decline. Within the MCI group, patients who progressed to dementia, we found higher whole brain atrophy rates (compared to MCI patients who remained stable), in analogy with their faster clinical decline.

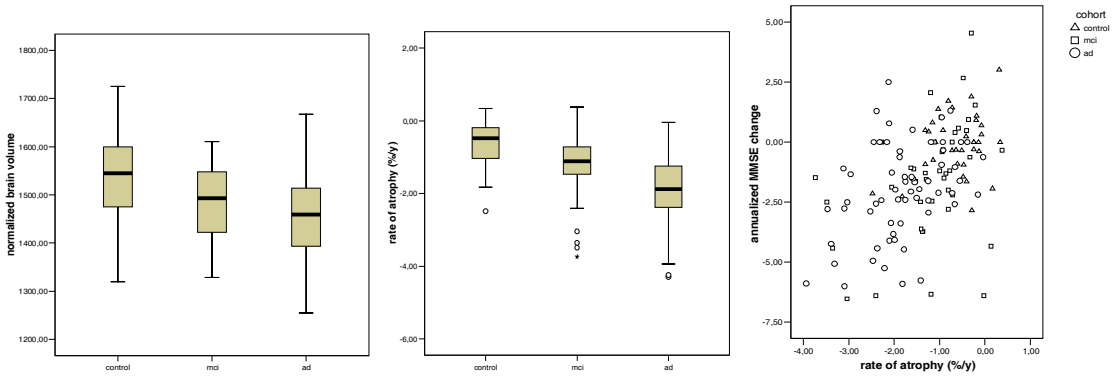

Fig 1 normalized brain volume (mL) for controls, MCI and AD
Fig 2 whole brain rate of atrophy (%/y) for controls, MCI and AD
Fig 3 correlation whole brain rate of atrophy (%/y) and annualized MMSE change (r=0.47)

References
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