CLINICAL RESEARCH STUDY

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Structural and Microstructural Brain Changes Predict Impairment in Daily Functioning

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ABSTRACT

BACKGROUND: Brain changes on magnetic resonance imaging (MRI) reflect accumulating pathology and have clinically disabling consequences, such as dementia. However, little is known on the relation of these MRI markers with daily functioning in nondemented individuals. We investigated whether structural and microstructural brain changes are associated with impairment in activities of daily living in a community-dwelling population.

METHODS: Between 2005 and 2009, 2025 stroke-free nondemented participants (aged 59.9 years) from the population-based Rotterdam Study underwent brain MRI, yielding global MRI markers, focal MRI markers, and microstructural MRI markers. We used the Stanford Health Assessment Questionnaire to assess basic activities of daily living, and the Instrumental Activities of Daily Living Scale to assess instrumental activities of daily living. Follow-up on activities of daily living was obtained between 2008 and 2013 (mean follow-up 5.7 years). We used linear regression to analyze continuous scores of daily living and logistic regression for incident impairment.

RESULTS: Eighty-two participants became impaired in basic and 33 in instrumental activities of daily living. Smaller brain and hippocampal volume and higher diffusivity were associated with larger change in activities of daily living. Smaller brain volume (odds ratio [OR] 4.05 per SD; 95% confidence interval [CI], 1.81−9.02), larger white matter lesion volume (OR 1.33/SD; 95% CI 1.02−1.72) and higher mean (OR 1.55/SD; 95% CI, 1.11−2.15), axial (OR 1.49/SD; 95% CI, 1.08−2.07), and radial diffusivity (OR 1.51/SD; 95% CI, 1.09-2.10) were associated with higher risk of impairment in basic activities of daily living.

CONCLUSIONS: In community-dwelling individuals, brain changes are associated with deterioration and incident impairment in daily functioning.

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KEYWORDS: Activities of daily living; Brain; DTI; Epidemiology; MRI

Normal aging and neurological diseases, such as dementia, are often accompanied by impairment in cognitive and daily functioning.[1] Previous studies have shown strong associations of poor cognition with worse daily functioning.[2-4] Moreover, cognitive decline is often accompanied by concurrent decline in daily functioning.[5] Despite

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this co-occurrence, it is primarily deterioration in daily functioning, rather than cognition, that leads to loss of independence and institutionalization. Therefore, unraveling determinants of daily functioning is important to understand processes leading toward loss of independence.

Structural brain changes, as visualized on magnetic resonance imaging (MRI), are strong determinants of cognitive impairment, even in nondemented subjects.[6,7] Recently, microstructural integrity of white matter, which is invisible on conventional MRI but can be quantified on diffusion tensor imaging (DTI), has also been shown to be associated with cognition.[8,9] Although the role of structural and microstructural brain changes in cognitive impairment is clear, little is known on their relation with daily functioning.

Generally, daily functioning is assessed by activities of daily living, including physical basic activities, such as eating, and more cognitive instrumental activities, such as meal preparation.[10]

Previous studies investigating brain changes in relation to activities of daily living were mainly clinic based.[3,11-13] Yet, public health impact is best evaluated in a community-dwelling population. Additionally, these studies rated structural brain changes visually, while automated quantification may disentangle more subtle associations.[3,11-13] Furthermore, study of microstructure may show whether brain pathology invisible on conventional MRI leads to deterioration in daily functioning.

We investigated whether structural and microstructural brain changes are associated with deterioration in basic and instrumental activities of daily living in nondemented community-dwelling individuals.

CLINICAL SIGNIFICANCE

- In nondemented community-dwelling individuals, structural and microstructural brain changes are associated with deterioration and higher risk of impairment in a wide range of daily activities.
- These associations were strongest for brain atrophy.
- Microstructural brain changes provide additional information above structural brain changes in predicting who will deteriorate in daily functioning.
- Brain changes may provide a valid intervention target to prevent future impairment in daily functioning.

METHODS

Setting

The study was embedded in the Rotterdam Study, a population-based cohort study.[14] In 1990 and 2000, all inhabitants of Ommoord, a suburb of Rotterdam, aged 55 years and older were invited to participate. In 2006, the cohort was extended, inviting all inhabitants aged 45 years and older. Every 3-4 years, participants are re-invited for follow-up examinations. At baseline and follow-up visits, participants undergo an interview, including activities of daily living questionnaires, and medical examinations. In August 2005, MRI scanning was included in the study protocol. The study was approved by the Medical Ethics Committee of the Erasmus MC. All participants gave written informed consent.

The current study is based on participants from the second and third sub-cohort of the Rotterdam Study, who underwent MRI scanning until September 2009. We invited 4595 participants for MRI scanning. We excluded individuals for dementia (n = 14), history of clinical stroke (n = 103), or MRI contraindications (eg, pacemaker or claustrophobia, n = 340). Of 4138 eligible subjects, 3794 agreed to participate. For 45 subjects, MRI scanning was not completed due to physical or technical problems, and 96 were excluded for artifacts, cortical infarcts, or large meningiomas.

Due to lack of personnel, the questionnaires were removed from the interview between February and August 2006, leading to 669 random subjects being excluded. In total, 2984 participants had complete and valid baseline data.

Follow-up assessment of daily functioning was performed between December 2008 and August 2013. Eighty-eight participants died before follow-up. Of the remaining participants, 2229 were re-invited, of whom 160 refused to participate, 21 did not respond, 11 were unable to participate, 9 had missing follow-up data, and 3 had moved out of the study area. Finally, we included 2025 participants in the analyses.

Our DTI protocol was implemented only in MRI scans of participants from the third sub-cohort (n = 1283).

MRI Acquisition and Processing

Brain MRI scanning was performed using a 1.5-tesla scanner with an 8-channel head coil (GE Healthcare, Milwaukee, WI), and included T1-weighted, proton-density weighted, fluid-attenuated inversion recovery-weighted, T2*-weighted sequences and DTI.[15]

Automated tissue classification based on a k-nearest neighbor classifier algorithm extended with white matter lesion segmentation was used to quantify supratentorial brain, gray matter, white matter, white matter lesion, and intracranial volume.[16,17] Total white matter volume was the sum of normal-appearing white matter and white matter lesion volume.

Hippocampus was segmented automatically based on an intensity model and a spatial probability map.[18]

Lacunar infarcts were rated as focal parenchymal lesions (3-15 mm in size) without involvement of cortical gray matter.[19] Microbleeds were rated as focal hypointensities on T2*-weighted sequences.[20]