Study Design: Amyloid Pathology In Cognitively Normal Elderly Twins

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Introduction
Alzheimer’s disease (AD) is a neurodegenerative disorder characterized by progressive neuronal loss and eventually death. Abnormal aggregation of beta amyloid (Aβ) is the first event in AD and is present in 20-40% of cognitively normal elderly (Figure 1). After Aβ aggregation neuronal injury develops. The concordance of monozygotic twins for a clinical diagnosis of AD-type dementia is 0.40-0.67. This suggests a major genetic role in the development of AD but also involvement of environmental factors.

Objectives:
1. To determine the concordance of Aβ and neuronal injury AD biomarkers and the combination of both in monozygotic twins
2. To analyze the appearance of AD biomarkers in relation to cognitive decline and/or diagnosis
3. To test whether discordance is associated with gene expression and DNA methylation

Methods: Cognitive testing and imaging
Longitudinal observational cohort study of 100 monozygotic twin pairs aged 60-100 years from the Netherlands Twin Registry (NTR) (Table 1).

After 2 years cognitive testing and questionnaires

Table 1: Baseline measurements in 200 cognitively normal elderly

Expected Results: Start December 2014
- Markers amyloid pathology: Aβ in CSF analysis and amyloid-PET scan.
- Markers for neuronal injury: tau & p-tau in CSF, neuropsychological and clinical markers, functional and structural brain connectivity measured by MEG and MRI, brain atrophy by MRI, vascular changes by MRI, retinal imaging and duplex of the carotid arteries

Conclusions
The degree of gene expression and DNA methylation markers will be compared between concordant and discordant twin pairs.