Amyloid pathology in the diagnosis and treatment of cognitive decline and dementia in patients with Down syndrome.

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To investigate the relation between the amyloid metabolism (as measured by plasma Abeta1-40 en 1-42) and the incidence of dementia in DS patients and the investigate whether there is interaction with vascular or genetic factors with respect to this...

Ethical review	Approved WMO
Status	Pending
Health condition type	Mental impairment disorders
Study type	Observational invasive

Summary

ID

NL-OMON30898

Source
ToetsingOnline

Brief title
Amyloid pathology and cognitive decline in Down syndrome.

Condition

- Mental impairment disorders

Synonym
cognitive decline, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW

Intervention

Keyword: amyloid, dementia, Down syndrome, magnetic resonance imaging

Outcome measures

Primary outcome

incidence of dementia (number of incident case per 100 persons year)

Secondary outcome

- change in cognitive performance (follow-up minus baseline).

- difference in serum amyloid between those that have or have not developed

dementia.

- difference in radiological characteristics between those that have or have

not developed dementia.

Study description

Background summary

Down syndrome (DS) is the most frequent cause of mental retardation and occurs in about 1 out of 1000 newborns. Due to improved medical care the life-expectancy of persons with DS has dramatically increased. Currently about half of all DS patients reaches the age of 60 years or over. Consequently, these patients are also being confronted with the consequences of ageing. Especially among DS patients one of the first manifestations of ageing is cognitive decline, ultimately resulting in dementia, most frequently of the Alzheimer*s disease type (AD). The overall prevalence of AD among DS patients is about 15%, while this is about 80% among those between 60-70 years. (the AD prevalence within this age-stratum is about 5% among patients without DS). The high prevalence makes dementia the most important risk factor for morbidity and mortality among DS patients.
The most common explanation for this observation is a gradual increase in the number of amyloid plaques in the brain because the amyloid encoding gene, the APP gene, is on the in DS triplicated chromosome 21.
However, not every DS patient becomes demented, however until now it is not

possible to predict who will become demented or who will not. Getting to know this may be very relevant since early intervention by for example cognitive training in the progression from cognitive decline towards dementia may be possible and postpone cognitive decline.
Two important predictive factors for the development of dementia have emerged from the literature namely amyloid metabolites and certain genotypes. It is now possible to measure the degree of *amyloid pathology* in plasma by the determination of the amyloid fragments Abeta1-40 en 1-42. A possible genetic factor that increases the susceptibility for AD could be the presence of an APOE4 allele. It has never investigated whether these factors also play a role in the prediction of AD in patients with DS. If so, than early determination of these factors could aid in the prediction of AD in patients with DS, still without cognitive deterioration.
It is not known how these factors may relate to dementia in patients with Down syndrome, but the occurrence of brain changes seem a plausible explanation. However to date, the radiological substrate of dementia in DS patients is unknown, while it has been characterized in great detail for AD patients (including hippocampal and cortical atrophy). Detailed knowledge on underlying radiological mechanisms on the structural changes involved in dementia in DS patients may provide a better insight on those DS who may develop DS or who will not.

Study objective

To investigate the relation between the amyloid metabolism (as measured by plasma Abeta1-40 en 1-42) and the incidence of dementia in DS patients and the investigate whether there is interaction with vascular or genetic factors with respect to this relation.
Secondly, we want to investigate whether the underlying radiological substrate of dementia among DS patients.

Study design

longitudinal cohort study.

Study burden and risks

To the best of our knowledge the burden and risks associated with participation is limited as all questionnaires and additional investigations used are used on a routine basis, also in patients with Down syndrome and outweighs the expected benefits of a better understanding of the etiology of cognitive decline in Down patients and possible treatment options this may have. As the objective of the study specifically addresses a research question within the "Down research field" this question can only be addressed by asking for the participation of patients with Down syndrome.
Due to the expertise of specialized physicians within the field of mentally

retarded people and people who guide the participants on a daily basis we will immediately be notified when a participants does not want to continue with the study.

The actual burden consists of some questionnaires, 1 time a blood withdrawal, routine physical examination and a MRI scan. These are routine investigations.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Down syndrome
- Participation with previous research of the collaborator of this study (Dr A. Coppus) because this proposal can be viewed as the successor of the previous work of Dr. Coppus and because some baseline determinants are important risk factors for our outcome.

Exclusion criteria

Dementia at the baseline study

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	384
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL18379.091.07