Evaluating blood biomarkers from healthy controls and patients with age*related disease: Alzheimer*s disease

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44366

Source
ToetsingOnline

Brief title
Biomarkers for Alzheimer*s disease and aging

Condition

- Other condition

Synonym
Alzheimer's disease, dementia

Health condition

Neurodegenerative disorders

Research involving
Human

Sponsors and support

Primary sponsor: Johnson & Johnson Pharmaceutical
Source(s) of monetary or material Support: Janssen Vaccines an Prevention BV (Janssen Prevention Center)

Intervention

Keyword: aging, Alzheimer's disease, biomarkers, elderly

Outcome measures

Primary outcome

The primary endpoints of this study are A*1*42/A*1*40 ratio, A*1*40, A*1*42,

NFL, t*tau and anti*tau antibodies in plasma

Secondary outcome

The secondary endpoint is the combination of biological age with AD markers.

Biological age will be calculated using measurements of FEV1, systolic blood

pressure, total cholesterol, C*reactive protein, cytomegalovirus IgG,

creatinine, urea nitrogen, alkaline phosphatase, albumin and glycated

haemoglobin.

Study description

Background summary

Current Alzheimer*s Disease (AD) diagnosis is based on clinical findings and can only be made after multidisciplinary consultation. Measurement of markers such as declining amyloid*beta (A*)1*42 and increasing total tau (t*tau) and hyperphosphorylated tau levels in cerebrospinal fluid (CSF) may support the diagnosis; however, CSF measurement is invasive, expensive and not easily accessible. There is thus a need for a
simple biomarker*based blood test, which could facilitate (early) diagnosis of AD. The biomarker(s) could contribute to the prevention of AD by elucidating the pathogenesis of AD. The test could also facilitate in exploring new interventions in clinical trials. AD increases significantly with age implying

that aging is an important risk factor for AD. However, people of the same chronological age, age differently. Using 10 physiological parameters correlated with chronological age, it is possible to calculate a latent variable called *biological age* able to predict mortality more effectively in 20 years of follow*up than chronological age alone.Therefore, in addition to studying the association of AD*specific biomarkers, this proposal will also include measuring biological age. Combining biological age with disease*specific markers may improve distinction between AD and non*AD subjects.

Study objective

The primary objective is to evaluate plasma levels of A*1*42/A*1*40 ratio, A*1*40, A*1*42, neurofilament light (NFL), t*tau and anti*tau antibodies as disease*specific markers for AD. The secondary objective is to measure biological age parameters (i.e. forced expiratory volume in 1 second [FEV1], systolic blood pressure, total cholesterol, C*reactive protein, cytomegalovirus IgG, creatinine, urea nitrogen, alkaline phosphatase, albumin and glycated haemoglobin) and determine whether the combination of biological age with AD markers
can make a distinction between AD and non*AD subjects.

Study design

A cross*sectional, observational study with invasive measurements (blood draw).

Study burden and risks

There are no direct benefits for the participants of the study. There is a single study visit during which 42.5 ml of blood (5 tubes) will be collected by venipuncture, and some non*invasive measurements are done: blood pressure, FEV1, weight, length and grip strength. Healthy controls are administered questionnaires to assess absence of cognitive complaints and standard physical examination to verify that they are healthy. The risk
associated with participation is negligible and the burden related to the study procedures can be considered minimal.
In this study patients are included that are recently diagnosed with AD and considered not incapacitated. As specified above, the risks are negligible and the burden is minimal. The topic of this study is markers for AD; this can only be tested in blood from AD patients and
therefore can only be done with these patients.

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

- Written informed consent
- Able to communicate well with the investigator in the Dutch language
- Aged 65-85 (including 85) years.;Additional for AD patients:
- New diagnosed with probable AD according to NIA-AA criteria
- MMSE score 18-26
- Imaging evidence to confirm absence of cerebrovascular damage or other neurodegenerative disorder
- Mentally competent for study participation as judged by treating physician and study physician.;Additional inclusion criteria for the healthy controls are:
- No memory complaints;
- MMSE score *27;
- 7MS total score < 0 (formula for total score calculation is described in Solomon et al.

1998);
- Considered healthy defined by absence of any active or chronic disease, based on medical history (self*reported) and physical examination.

Exclusion criteria

Exclusion criteria for AD subjects are:
- Diagnosis of genetically proven familial AD
- History of concussion or other acute head trauma in the past six months;
- Current or past diagnosis of autoimmune disease;
- Current or past diagnosis of immunosuppressive disorder;
- Ongoing or past (within the last 3 months) treatment with any immunosuppressive drug (e.g. prednisone);
- Recent (within the last 3 months) transfusion or treatment with blood products such as intravenous immunoglobulins;
- Ongoing or past (within the last 3 months) treatment with drugs (e.g. Anakinra) that suppress the interleukin*1, interleukin*6, or TNF** response EXCEPT non*steroidal anti*inflammatory drugs;
- Current or previous (within the past year) treatment for malignancy;
- Current or previous (within the past year) diagnosis of hematological malignancy;
- Recent (within last 3 months) surgery;
- Recent (within last 2 weeks) acute infection.;Exclusion criteria for healthy elderly:
- Current diagnosis of probable dementia of any etiology;
- Current or past diagnosis of clinically significant pulmonary, cardiovascular, endocrine, hematologic, neurological, immune, gastrointestinal or genitourinary disease or cancer;
- Recent (within last 3 months) surgery;
- Recent (within last 2 weeks) acute infection;
- Taking any prescription drugs within 14 days of the study day or within 5 times the elimination half*life of the medication (whichever is longer). Occasional acetaminophen/paracetamol use and statins (if given as primary prevention) are allowed. Exceptions may apply when, judged by the investigator, use of concomitant medication does not interfere with the study objectives.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-10-2017
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	28-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL62498.056.17