Age and performance: the relation between brain structure and cognition.

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The goal of this project is to elucidate the relation between structural differences in the brain and cognitive performance in younger and elderly participants. By utilizing the strength of high spatial resolution MRI we will compute measures of...

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

Summary

ID

NL-OMON47309

Source
ToetsingOnline

Brief title
Brain structure and cognition

Condition

- Other condition

Synonym
n.v.t.

Health condition

geen aandoening

Research involving
Human

Sponsors and support

Primary sponsor: Rijksuniversiteit Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: aging, brain structure, cognition, MRI

Outcome measures

Primary outcome

The main study parameters can be divided into parameters related to the MRI scans and parameters related to the cognitive tests.

MRI scans:

T1- and T2-FLAIR weighted scans will be used to derive volumetric data, measures of cortical thickness and percentage of white matter hyper intensities (relative to the total volume).

Volume measures will be derived from the scans with regard to the following areas: 1) prefrontal cortex (grey matter); 2) right thalamus; 3) hippocampus; 4) left dorsolateral prefrontal cortex; 5) pre-SMA (grey matter) and 6) whole brain (grey matter). Cortical thickness in the following regions of interest will be calculated: 1) left superior frontal gyrus; 2) left anterior inferior temporal cortex; 3) right superior and middle frontal gyri. The percentage of white matter hyper intensities will be computed for the whole brain (percentage in relation to total brain volume).

The DTI scans will be used to calculate the fractional anisotropy (FA) value of the following regions of interest: 1) splenium; 2) anterior part of the

inferior fronto-occipital fasciculus; 3) occipital lobe white matter; 4) parietal lobe white matter and 5) prefrontal cortex. Additionally the mean diffusivity (MD) value of the anterior part of the brain will be computed.

Cognitive tests:

The primary analysis considers the outcome measures of the 15 word test, the Simon task and the TMT. The TMT outcome measure consists of the time needed to perform part B of the test divided by the time needed to finish part A. The outcome measure of the Simon task is the mean reaction time on incongruent trials minus the mean reaction time on the congruent trials (the so called Simon effect).The 15 word test outcome measure of interest is the delayed recall score (number of words remembered 15 minutes after imprinting) will be used.

Secondary outcome

For the secondary analyses the following parameters are of interest:

MRI scans:

From the T1- and T2-FLAIR weighted scans we derive the following main parameters for each participant: 1) volumetric data of grey matter, white matter and cerebral spinal fluid; 2) (mean) cortical thickness and 3) percentage of white matter hyperintensities in relation to the total brain volume. All parameters will be calculated for the whole brain and for the prefrontal cortex separately. The main parameters that will be derived from the DWI images are mean DTI scalar values (FA, MD, AD and RD) for the

prefrontal cortex (division is made based on the FreeSurfer Brain Atlas) and the following white matter tracts (localized by tractography): the Uncinated Fasciculus, Splenium and Genu of the Corpus Callosum and the Cingulum.

Cognitive tests:

Main study parameters of cognitive performance consist of the default outcome measures of each cognitive task for each participant. For computer tasks these consist of: speed and accuracy. For the paper-pencil and verbal tests the main parameters consist of: number of correct words and repetitions (fluency), number of correctly pronounced words (crystallized intelligence) and number of items correct (fluid intelligence and mental imagery). Regarding outcome measures obtained in the driving simulator average speed, lateral road position and deceleration of a following car are analysed. In addition, heart rate (variability) as an indication of mental effort will be examined.

Study description

Background summary

In general ageing is related to changes in cognition, however, what is fascinating, is that there seem to be large individual differences in this process (Saliasi et al., 2015, Mungas et al., 2010). With this study we aim to broaden our understanding of the mechanisms that underlie the differences in age-related effects on cognition.

Widespread structural changes have been observed in the ageing brain (Raz & Kennedy, 2009). However, although structural integrity of the brain is crucial for cognitive performance, studies that found direct links between age, cognition and brain structure are limited and findings have been inconsistent (Park & Reuter-Lorenz, 2009). The neuropsychological perspective as described by van Petten (2004) and Westlye and colleagues (Westlye, Grydeland, Waldhovd &

Fjell, 2011) suggests that age related cortical atrophy drives the correlation between brain and behavior.

One of the disadvantages of the research done so far, is that studies examining the relationship between age, brain structure and cognition, mainly focused on specific cognitive functions. Considering the large inter-individual difference in age-related effects on cognition, we argue that it is of great importance to consider a broader spectrum of cognitive abilities instead. The main aim of our proposed study is therefore to explore the structure-function relationship in young and elderly adults, using an extensive neuropsychological test battery covering a broad spectrum of simple to complex cognitive abilities

During primary analysis we will explore the influence of age on the relation between cognitive task performance and structural characteristics of the brain focussing on three cognitive tasks that tax different cognitive functions and are often used in this type of research. Therefore they lend themselves for specific hypothesis testing. Performance on a verbal memory task (15 word test), an inhibition task (Simon task) and a task of cognitive flexibility (Trail Making Test) will be assessed in a young and elderly group and related to structural brain predictors based on previous literature. Indicators of brain structure and structural connectivity will be obtained through Magnetic Resonance Imaging (MRI). We will first assess whether previously found relations between specific structural brain measures and cognitive performance replicate and in addition, to what extent these measures distinctively contribute to explaining the cognitive performance. By comparing two age groups we will be able to examine the influence of aging on the relation between brain structures and cognitive functioning. In secondary analysis we will use the entire set of tasks and relate these to structural brain measures by means of principal covariates regression.

Study objective

The goal of this project is to elucidate the relation between structural differences in the brain and cognitive performance in younger and elderly participants. By utilizing the strength of high spatial resolution MRI we will compute measures of structural brain characteristics and map connections between brain areas. By relating these outcome measures to performance on a broad spectrum of cognitive tests, we seek to examine the influence of age on the relation between brain structure and cognitive performance.

Primary Objective: Investigate the effect of age on the relation between structural characteristics of the brain and cognitive performance.

Secondary Objective: Assess the relation between structural characteristics of the brain and a broad spectrum of cognitive tasks by means of an exploratory approach.

Study design

The study combines high spatial resolution MRI data and behavioural measures of cognitive performance in young and elderly adults. Participants will be screened for general cognitive functioning by means of the Montreal Cognitive Assessment (MoCA), a screening tool for Mild Cognitive Impairment. Data is collected at two separate days, on day 1 participants perform the cognitive tasks and on day 2 the MRI scan is made. Additionally participants fill out a set of questionnaires at home beforehand, providing information on possible confounding variables.

During day 1, participants will perform different cognitive tasks covering a broad spectrum from simple to complex cognitive abilities. These tasks are: 1) reaction time task; 2) selective and divided attention task; 3) inhibition task; 4) visual observational ability task; 5) working memory task; 6) semantic and phonetic fluency tests; 7) 15 words test (verbal memory); 8) trail making test (i.a. conceptual tracking ability); 9) Dutch reading test for adults (crystalized intelligence); 10) WAIS matrices (fluid intelligence); 11) Clock test (mental imagery manipulation) and 12) a driving simulator task.

During day 2 MRI data will be collected in a 3 Tesla Siemens MRI scanner. The scanning procedure contains a T1- and T2-FLAIR weighted scans and a DWI scan. During scanning the participant is asked to lie as still as possible and to relax as no specific task has to be exerted during scanning.

Participants will be fully informed about the nature and parameters of the study and paradigm before the experimental sessions and after the second session they will be fully debriefed.

Study burden and risks

In the MRI-scanner participants will be exposed to a field-strength of 3 Tesla and scanner noise. Thus far there is no evidence to suggest that exposing human to a magnetic field of this strength has a negative influence on health. With regard to the noise, ear protection will be provide. Participants will not benefit directly from participating in the study, however the data collected during this study will enhance our understanding of the relationship between structural brain differences and cognitive performance in ageing.

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

- aged 18-25 or 60-70 years old
- right-handed
- normal (or corrected to normal) vision
- having signed the informed consent
- having a drivers licence for cars
- older group: working in a paid job for at least 20 hours a week at the moment of participation in the study and in the 5 years preceding participation
- younger group: spending at least 20 hours a week on full-time education
- gender will be matched between the groups, so that the same proportion of each is present in both groups.

Exclusion criteria

- not matching the inclusion criteria
- MR incompatable (posibility of any incompatible metal objects inside the body)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-04-2017
Enrollment:	132
Type:	Actual

Ethics review

Approved WMO Date:	05-01-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL56698.042.16