Language decline in subjective cognitive impairment: Early detection of dementia

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Our project aims to investigate cognitive and linguistic deficits in people with SCD, focusing on working memory impairments, deficits of lexical access, and deficits brought on by syntactic complexity. We will integrate clinical linguistic findings...

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

Summary

ID

NL-OMON57339

Source
ToetsingOnline

Brief title
Early detection of dementia

Condition

- Other condition

Synonym
cognitive impairment, dementia, language decline, MCI, SCD

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Eerste geldstroom (geld van Ministerie van OC&W aan universiteiten)

Intervention

- No intervention

Keyword: Functional Near-Infrared Spectroscopy (fNIRS), Language and cognition, Mild Cognitive Impairment (MCI), Subjective Cognitive Decline (SCD)

Explanation

N.a.

Outcome measures

Primary outcome

<p>N-back task is a popular measure of working memory involving an activation of
the FPN (Mencarelli et al., 2019). A metanalysis showed age-related decline in
n-back performance where accuracy decreases and response time increases as the
load increases (Bopp & Verhaeghen, 2018). In this study, we will use three
different load factors (i.e., 0, 1, and 2) in order to explore the difference
in performance as well as related neuroimaging and eye-tracking measures
between healthy, SCD, and MCI groups.

Three language tasks will be employed: action and object naming, comprehension
of passive and active reversible and irreversible sentences, as well as
elicited imitation of complex sentences. Since an impairment in action naming
due to reduced lexical access to verbs has been described (Macoir et al.,
2019), the naming test will be administered consisting of 48 object and 48
action pictures. Sung et al. (2020) found a sentence comprehension deficit in
the MCI stage when the syntactic complexity was increased (passive sentences).
This is why we will test the comprehension of passive and active sentences,
including 128 sentences, matched for frequency, age of acquisition,
concreteness, word length, and valence. The last language task administered
will be the Elicited imitation (Lust, Flynn and Foley 1996) of complex
sentences used in the Sherman et al. (2013) study, including coordinated
clauses and relative clauses, varied according to syntactic and semantic
factors. The participants will be asked to repeat the sentences they hear.
fNIRS + EEG
The fNIRS cap will be placed on the participants* head. Concentration changes
of oxygenated (oxyHb) and deoxygenated (Hb) haemoglobin will be recorded using
NIRS. Sources and detectors will be distributed on the Broca*s and Wernicke*s
area.

Main parameters/outcomes:
- Differences in HBO levels during all four tasks (F test; GLM; analysed using
NIRS Toolbox), group comparisons
- Change in fronto-parietal EEG synchronisation: n-back, and linguistic tasks

(Fieldtrip EEG Toolbox, non-parametric statistical analyses).
- Topographical EEG power changes (resting state EEG) and ERP effects during
linguistic tasks.
- D-prime (signal detection) analysis - N-back task.
- Accuracy and/or RTs - linguistic tasks.

Secondary outcome

1. Correlation of verbal fluency and language performance.
2. Correlation between executive functions and language performance.
3. Correlation of pupil dilation measures and performance during cognitive and
linguistic tasks.

Study description

Background summary

Subjective cognitive decline (SCD) is a form of self-reported cognitive impairment and one of the early predictors of Alzheimer*s disease, preceding objective mild cognitive impairment (MCI) (Jessen et al., 2020). In recent years, SCD has been put into focus due to its importance for early detection of Alzheimer*s disease (AD), as well as the current neuropsychological tools* lack of sensitivity to SCD. While it is often possible to detect early AD using biomarkers, lumbar puncture, PET, and MRI (Jack et al., 2010), these tests are considered to be highly invasive, extremely expensive, and not widely available (Johnson et al., 2012). This is why it is important to find and design more affordable, accessible non-invasive methods for early detection of dementia. Subjective complaints do not always correlate with objective cognitive performance (Jungwirth et al., 2004). People with SCD seem to perform similarly on the n-back task as those without subjective complaints, but they do show distinct hemodynamic response (Zhang et al., 2021). Neuroimaging studies have shown some promise in documenting potential markers of SCD (Parker et al., 2022). For instance, Kawagoe et al (2019) reported a positive correlation between complaint severity and parieto-occipital connectivity. However, more research is needed to confirm this evidence. Additionally, Marandi and Gazerani (2019) argued that eye tracking is a promising tool to provide objective biomarkers of aging and neurodegeneration. In particular, pupil dilation has been shown to be related to prefrontal activation during a working memory task (Yeung et al., 2021).
Language deficits have been reported for AD and aMCI. They include impaired lexical access, impaired semantic fluency (Belleville et al., 2017) and sentence level complexity (López-Higes et al., 2014; Sung et al., 2020), reduced discourse cohesion, *empty speech*, and paraphasias. However, when it comes to SCD, studies focusing only on language impairments are not numerous

and they focus mostly on verbal fluency. Authors have used lexical access tasks to compare participants with SCD to healthy aging elderly and participants with MCI and AD (Benito-Leon et al., 2010; Ostberg et al., 2005).

Study objective

Our project aims to investigate cognitive and linguistic deficits in people with SCD, focusing on working memory impairments, deficits of lexical access, and deficits brought on by syntactic complexity. We will integrate clinical linguistic findings with brain activation measured by fNIRS and EEG, and pupil dilation measured by eye-tracking. This will be a longitudinal study with a 1-year follow-up. In this way, we plan to create a neurolinguistic profile of SCD using neuropsychological and neuroimaging data.

In this study, we hypothesize that:
1. Older adults with SCD will perform better on n-back task as compared to those with MCI, but similarly to healthy controls (HC).
2. Older adults with SCD will show greater connectivity of the frontoparietal network (FPN) connectivity than HC and people with MCI, indicating a compensatory cognitive effort (Si et al., 2020).
3. Similarly, older adults with SCD will also show greater pupil dilatation changes than HC and people with MCI.
4. Action naming will cause bigger lexical access difficulties in individuals with SCD and MCI than HC, due to greater reliance on executive functions and attentional control (Macoir et al., 2019). Prediction: HC < SCD < MCI.
5. Linguistically more challenging structures (passives and relative clauses) will be more sensitive to cognitive decline. We predict that the SCD group will demonstrate more difficulties with complex sentence processing than HC, but less difficulties than the MCI group.

Study design

This will be a longitudinal observational study of brain activation while doing cognitive and linguistic tasks using fNIRS and EEG measurements, as well as pupillometry. Cognitive screening and language assessments will be separated and administered in two days to the three groups participating in the study. Groups needed for this study are: healthy elderly (healthy controls), elderly with subjective cognitive decline (SCD), and elderly with mild cognitive impairment (MCI). The same procedure will be used in the follow-up, a year later.
On day 1, the participants will be given the information about the assessments administered on this day, which include cognitive screening and a short spontaneous speech interview. This usually takes around 60 minutes.
The cognitive screening will include:
o Mini-Mental State Examination (MMSE)
o 15-Word Test (15WT)

o Trail-Making Test (TMT)
o Stroop Color-Word Test (SCWT)
o WAIS Digit Span
o WAIS Symbol Digit Modalities Test (SDMT)
As well as:
o Geriatric Depression Scale-30 (GDS-30)
o Apathy Evaluation Scale (AES)

o Spontaneous speech

On day 2 cognitive and linguistic tasks will be administered. Since a more sensitive way to measure language processing is required, functional near-infrared spectroscopy (fNIRS) and electroencephalography (EEG), which allow for real-time measurement of neural activity, and eye-tracking (pupillometry) will be used to support the study and capture subtle changes.
Before the four tasks are administered, the resting state EEG will be done. This will entail a 2-minute eyes open/ 4-minute eyes closed' protocol, lasting 6 minutes in total.
Tasks
In the current study, one cognitive and four linguistic tasks will be administered:
(I) N-back task
(II) Object and action naming,
(III) Elicited imitation of complex sentences,
(IV) Comprehension of reversible and irreversible active and passive sentences.

Intervention

Not applicable.

Study burden and risks

The study will consist of two sessions: the first for a 5-minute spontaneous speech interview and neuropsychological testing - screening whether all inclusion criteria are met (and no exclusion criteria). This will usually take no longer than 60min. The second session concerns the resting state and cognitive and linguistic testing using fNIRS, EEG, and eye-tracking measurements, with a total duration of around 90 min. After a year, Session 1 and Session 2 will be repeated (YFUs1 and YFUs2).

The experiment will not involve more than minimal risks for the participants. NIRS, EEG, and pupillometry are standard non-invasive brain activation measuring techniques with no known negative effects on health. The study is not intended to benefit the participants directly. Participants will receive compensation/a present for their contribution.

Contacts

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Trial sites

Trial sites in the Netherlands

Universitair Medisch Centrum Groningen
Target size: 120

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Age >=50 years
Right-handedness
Diagnosis of aMCI based on neurologist evaluation or subjective cognitive complaints with no official diagnosis.
aMCI will be defined as having a verbal memory score 1.5 standard deviations

below the normative control values on both sub-scales.
Signed written informed consent.

Exclusion criteria

1. History of psychiatric or neurological illness other than MCI (exception is for depression in MCI group as it is co-morbid with MCI)
2. Excessive intake of alcohol (>2 units per day)
3. Drug abuse
4. Severe scalp skin lesions
5. Color blindness

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Other type of control
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	28-04-2025
Enrollment:	120
Duration:	12 months (per patient)
Type:	Anticipated

Medical products/devices used

Product type:	N.a.

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	04-03-2025
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-05-2025
Application type:	Amendment
Review commission:	METC UMCG

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	NL86354.042.24
Research portal	NL-005122