Vitamin D status and cognitive functioning in patients with relapsing remitting multiple sclerosis * a neuropsychological and functional MRI approach

Published: 04-08-2011
Last updated: 29-04-2024

Primairy objective:* To assess whether a poor vitamin D status in RRMS patients is negatively associated with cognitive performance in neuropsychological tests (information processing speed and working memory) and with measures of cognitive (dys)...

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

Summary

ID

NL-OMON36084

Source
ToetsingOnline

Brief title
Vitamin D status and cognition in MS

Condition

- Autoimmune disorders
- Demyelinating disorders

Synonym
MS, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: gedeeltelijke ondersteuning door het Nationaal MS fonds

Intervention

Keyword: Cognitive functions, functional MRI, relapsing remitting MS, vitamin D

Outcome measures

Primary outcome

Psychometric assessments prior to MRI assessment:

* Paced Auditory Serial Addition Test (PASAT)

* Symbol Digit Modalities Test (SDMT)

Functional MRI assessments:

* Task related fMRI, using the Sternberg paradigm (working memory function)

* Resting State fMRI, functional network integrity

* DTI, structural network integrity

* MR Spectroscopy, assessment of neurotransmitters GABA and glutamate

Serum sampling for assessment of:

* Vitamin D status (25(OH)D serum level)

* Vitamin B12 status (Cobalamin serum level)

- Cytokines in serum

Secondary outcome

Psychometric assessments:

-Fatigue will be measured with the Fatigue Severity Scale (FSS)

-Depression will be measured with the depression-subscale of the hospital

anxiety and depression scale (HADS)

-Premorbid intelligence will be measured with the Nederlandse Leestest voor

Volwassenen (NLV)

Conventional MRI assessments:

-T1-weighted images, for volumetric assessment (atrophy)

-T2-weigthed FLAIR acquisition for lesion load assessment

-Double Inversion Recovery (DIR), cortical lesion assessment

Study description

Background summary

Vitamin D is traditionally considered as exclusively important for calcium homeostasis. Recent years, other biological functions of vitamin D gained attention. In multiple sclerosis (MS), a poor vitamin D status has been associated with an increased hazard on relapses, and with an increased amount of MS disability. However, other symptoms of MS have also been associated with vitamin D status. We found that a poor vitamin D status correlated negatively with the presence of depressive symptoms in MS. Recently, a prospective longitudinal cohort study in healthy elderly showed an association between a poor vitamin D status, and an increased hazard on cognitive decline. Cognitive impairment is also a frequent and disabling symptom, which is even found in early MS. Additionally, functional MRI analysis revealed subtle changes in connectivity and functional organization, indicating compensatory reorganization. This was especially observed in patients lacking severe cognitive complaints. In this project, we will explore the link between vitamin D status and signs of cognitive impairment in MS.
This research is important, because cognitive impairment is very common and interferes with the overall quality of life in MS patient. Until now, there is no treatment available for cognitive impairment and vitamin D supplementation might provide a cheap and safe preventive agent/ treatment. Therefore, identifying cognitive impairment as a potential target of vitamin D therapy could warrant inclusion of this parameter as outcome measure in clinical

trials.

Study objective

Primairy objective:

* To assess whether a poor vitamin D status in RRMS patients is negatively associated with cognitive performance in neuropsychological tests (information processing speed and working memory) and with measures of cognitive (dys)function on functional MRI (connectivity analysis).

Secondary objectives:

* To assess whether vitamin D status in RRMS patients is negatively associated with the presence of more severe depressive symptoms.
* To assess whether vitamin D status in RRMS patients is negatively associated with the presence of anxiety.
* To assess whether vitamin D status in RRMS patients is negatively associated with the presence of more severe fatigue.
* To assess whether vitamin D status in RRMS patients is negatively associated with a higher T2 lesion load.
* To assess whether vitamin D status in RRMS patients is negatively associated with a reduction in total brain volume.
* To assess whether vitamin D status in RRMS patients is negatively associated with an imbalance of neurotransmitters as measured by MRI spectroscopy.

Tertiary objectives:

* To explore the correlation of vitamin B12 status with the variables presented above.
* To explore the correlation between all the variables above.
- To explore the correlation between inflammation in serum and depression score

Study design

This is a two-arm cross-sectional study in which we will selectively include subjects with a poor (<50 nmol/L; N = 15) and high (>100 nmol/L; N = 15) vitamin D status (serum 25-hydroxyvitamin D levels).

Study burden and risks

Participating patients will have to participate in neurological examination and are asked to cooperate with neuropsychological tests. Additionally, they will have to cooperate with the MRI assessment, in which patients are asked to be as quiet as possible. This will take approximately 2 hours. Besides that the

assessments can be more or less fatiguing to the patients, there are no risks of these assessments. Finally, patients will donate blood 1 time. The risks of a blood donation are a temporary vasovagal reaction or a local haematoma at the puncture spot.

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

- A definite, MRI-confirmed, RRMS (Polman et al., 2005);
- A disease duration since the onset of first symptoms of *5 years;
- An age of 18-50 years;
- Treatment with either IFN-beta (Avonex, Betaferon, Rebif) or Glatiramer Acetate (Copaxone) or no disease modulating drugs (DMD) treatment;
- No exacerbation within 6 weeks prior to assessment;

- Vitamin D supplementation <<=20 *g/d (800 IU/d);
- A serum 25-hydroxyvitamin D (25(OH)D) level available within 1 year prior to inclusion, being either <50 nmol/L OR >100 nmol/L.

Exclusion criteria

- Progressive disease without relapses;
- Treatment with any immune suppressive or immune modulating drug or than IFN-beta or Glatiramer Acetate within 3 months prior to assessment;
- Cognitive dysfunction reported by spouses, family or MS nurses, neurologist or reported by previous neuropsychological research
- Presence of a depression as detected with the HADS (depression score *8;
- Vitamin D supplementation more than 20 *g/d (800 IU/d);
- Severe visual and/or verbal limitations interfering with neuropsychological testing;
- Contraindications for MRI examination.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-02-2012
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	04-08-2011
Application type:	First submission

Review commission: METC Z: Zuyderland-Zuyd (Heerlen)

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	NL36446.096.11