The effect of simvastatin on the cognitive deficits of children with Neurofibromatosis I (NF1): a randomized, double-blind placebo-controlled study.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21351

Source
NTR

Brief title
NF1 simvastatin trial

Health condition

Neurofibromatosis type 1 is the most common single gene disease causing learning disabilities in humans. Children with NF1 commonly have cognitive dysfunctions like learning and attention deficits as well as impaired motor coordination. Half of the children seen at the multidisciplinary NF1 outpatient clinic of the Sophia Children's Hospital attends special education.

Sponsors and support

Primary sponsor: Erasmus MC afd. Neurowetenschappen, Dr. Y. Elgersma
Source(s) of monetary or material Support: Sophia Kinderziekenhuis Fonds

Intervention

Outcome measures

Primary outcome

1. Performance on neuropsychological tests on visuospatial memory and attention after 1 and 3 months (Rey Complex Figure test (recall), Bourdon Vos Test);

2. Performance on neurofysiological tests on adaptation of movements after 1 and 3 months (saccade-adaptation test, adaptation of eye-hand coordination);

3. Measurement of the size, number, localization and spectra of UBO's (unidentified bright objects, hyperintensities on T2 weighed MRI), on T2 MRI and 3D CSI 1H-MRS after 3 months.

Secondary outcome

1. Score on the following neuropsychological tests after 1 and 3 months (after 1 month = under METC review):

1a. Judgement of line orientation test;

1b. Rey Complex Figure Test (copy);

1c. Beery VMI Test;

2. Score on the following neuropsychological tests after 3 months:

2a. IQ-test: WISC-RN;

2b. Verbal Fluency Test;

2c. Trailmaking Test A&B;

2d. Wisconsin Card Sorting Test;

2e. Peabody Picture Vocabulary Test;

2f. Boston Naming Test;

2g. 15 Word-Test;

2h. Stroop Color Word Test;

3. Identification of facial emotions (ANT)
Outcome of the following questionnaires after 3 months:

3a. Child Behavior Check List (CBCL parents);

3b. Teacher Report form (TRF);

3c. Child Behavior Check List (CBCL child);

3d. Quality of Life Questionnaire CHQ-CF87 Dutch edition (child) (under METC review);

3e. Quality of Life Questionnaire CHQ-PF50 Dutch edition (parents) (under METC review);

4. Performance on the following neurophysiological tests after 1 and 3 months:

4a. Basic saccade performance;

4b. Smooth pursuit.

Study description

Background summary

Recent research has shown that the cognitive phenotype of NF1 +/- mice can be reversed by the administration of statins. Because the majority of children with NF1 suffer from learning disabilities, statins could potentially make a large difference in the morbidity associated with NF1.
In a double-blind, randomized placebo-controlled trial, 60 children with NF1 are treated with simvastatin or placebo for three months. The effect of simvastatin treatment will be evaluated using neuropsychologic, neurophysiologic and radiologic parameters.

Study objective

Statin-treatment has been shown to normalize the learning- and attention deficits in NF1 +/- mice by decreasing Ras activity. The fact that statins are effective in NF1 mice, combined with their very good
safety profile, makes them an ideal candidate drug to treat cognitive impairments associated with NF1 in human patients.

Study design

N/A

Intervention

Simvastatin (10 mg/d for month 1, 20 mg/d month 2, 20 mg/d month 3 for children 8-12 years old or 40 mg/d month 3 for children 12-16 years old) or placebo once a day.

Contacts

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Eligibility criteria

Inclusion criteria

Children aged between 8 and 16 years, NF1 diagnosis according to the criteria of the National Institutes of Health, visiting the multidisciplinary NF1-outpatient clinic at the Erasmus MC – Sophia Children's Hospital; informed consent .

Exclusion criteria

Pathology of the CNS (hydrocephalus, epilepsy, radiotherapy, neurosurgery, etc.), deafness and/or severely impaired vision, use of anti-epilepics and/or neuroleptics.

Additional exclusion-criteria (under METC review):

a. Insufficient cognitive abilities to obtain a reliable score on a verbal IQ test (WISC-RN);

b. Contra-indications for simvastatin-treatment;

c. Planned hospitalization within three months after planned date of inclusion.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-01-2006
Enrollment:	60
Type:	Actual

Ethics review

Positive opinion

Date:	28-11-2005
Application type:	First submission

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
NTR-new	NL499
NTR-old	NTR542
Other	: N/A
ISRCTN	ISRCTN14965707

Study results

Summary results
http://www.ncbi.nlm.nih.gov/pubmed?term=18632543