Partial training-induced recovery of visual function in hemianopic patients after stroke

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

Summary

ID

NL-OMON35381

Source
ToetsingOnline

Brief title
Partial recovery of vision in hemianopia

Condition

- Other condition

Synonym
stroke; CVA

Health condition

beroerte

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: ZonMW / InZicht

Intervention

Keyword: MRI, stroke, training, visual field defects

Outcome measures

Primary outcome

Post-Pre differences in the measured variables (perimetry = subjective extent of the visual field; fMRI = objective extent of the visual field; structural MRI = connectivity between visual cortical areas; driving performance in the simulator; reading test) all provide an effect parameter of the full training (control and test training). These effect pairs collected for the 4 groups of subjects allow for univariate analysis of the main dimensions of the experiment: training (test or control) and training stimulus type (flow and points) and their interactions.

The effects of the control training (of the intact field) by itself and the test training (of the field defect) by itself are derived from Intermediate-Pre differences and Post-Intermediate differences. These differences are collected for each patient and thus allow for comparing between the two types of training on the effect parameters (perimetry, MRI measures, driving) using t-tests based on the full group size of 40 patients.

Secondary outcome

Secondary outcomes of this study are threefold:

(1) QoL questionnaires and (G)oal (A)ttainment (S)caling eveluate the change

in daily life performance following the training

(2) Evaluation of the trainingdata will provide insight in the frequency of

fixation loss during training and the change of the visual field defect during

the training; this may extend our insight into optimal duration of training.

(3) Loci with marked reduction of the field defect will be used to seek for

correlates in the structural MRI data prior to training, pointing e.g. to

special connectivity between intact field loci in higher visual cortex and

corresponding damaged visual cortical areas; and to seek for activity that

corresponds to areas that are subjectively blind prior to the training (i.e.

discrepancies between objective and subjective perimetry). This may help to

establish the odds of training outcome from MRI data prior to training.

Study description

Background summary

Annual incidence of cerebral infarctions or stroke is estimated at 41000 in the Netherlands (source: hartstichting.nl); some 30% remain visually impaired after the event. Only in this country we estimate some 50000 patients with visual defects after a CVA can be found. These numbers are likely to increase as our life expectancy increases and post-stroke care improves. Patients with cortical blindness have damage to the postgeniculate optic pathways, which results in a reduction of vision in the same part of the visual field of both eyes.
Different localization, size, and cause of damage result in various visual field disorders. Visual field defects may vary between an absolute hemianopic loss, to a relative loss where vision is partly impaired. Such field defects can seriously interfere with daily life activities like reading, recognition (of familiar persons, locations or objects) mobility (disorientation, stumbling

into objects, loss of a driving licence), and job security. Full spontaneous recovery occurs rarely.
Long after the event causing the defect, an assiduous visual rehabilitative training can reduce the field defect significantly in a part of the patients. The training effort is considerable for the patient, hence any gain of the efficacy of the training is desirable.

In our (and others') previous studies, about 70% of the patients shows a reduction of the visual field defect ranging from a few to tens of degrees. In about half of the cases the reduction of the defect is accompanied by significant behavioural improvements in reading and visual navigation. Although these results are important indicators of success the mere fact that in about half of the patients the training causes significant field enlargement leaves ample room for improvement. Can we then increase both the number of successfully trained patients as well as the magnitude of the visual field recovery?

We identify three potential causes for non-response to the training: (1) the stimulus is not effective enough (2) the patient is not effectively training at home because he/she does not fixate properly (3) the damage to the cortex is so deep and complete that there are only few sites along the field defect that contain potentially trainable remainders of circuitry.

ad 1) Our earlier studies indicate that reduction of the visual field defect by itself can lead to behavioural improvements only if the extent of the recovered field is sufficiently large. The extent that is required depends on the eccentricity of the defect: at higher eccentricity more degrees of visual field must be recovered to improve reading or visual navigation. Thus the standard training protocol (using single point targets) may be not particularly effective when the visual defect is eccentric. In case, a point target stimulates only a fraction of the retinal region that needs to be recovered by training!
ad 3) So far, we have very little means to predict whether a training effort will be successful. It is likely that cortical structure in the border region of the defected field is important for recovery, because we have found that the recovery shows a very gradual spatial shift of the visual field border(Bergsma et al. 2009). Thus, can we find neurobiological measures of change following training and derive from these correlates to visual field recovery and behavioural improvements? This may give important leads as to which particular structural changes relative to initial state in the border region of the defect are indicative of recovery potential.

Study objective

Previously we have shown that visual field defects in hemianopes can be reduced by visual training and that it improves performance in daily life activities like reading, car driving (in a simulator), and stimulus identification. Not all patients profit from the training effort. This project aims to develop the training protocol further to offer patients a better chance of visual field recovery and a larger extent of the recovery.

Four goals can be distinguished within this overall perspective.
(1) To find a more efficient stimulus for training than the previously used standard procedure of using point targets
(2) To improve the training efficiency at home by patients, by control and feedback of the patient's eye fixation
(3) To collect a broad range of objective MRI measures to follow the effects of the training on the defect and compare these with a series of behavioural and perceptual effects of the training
(4)To evaluate the impact of the field recovery on daily life activities.

These data are needed to identify cortical regions/connections that modify by training and regions that have e.g. functional activity that correspond to the defect; i.e. cortical visual responsiveness without reaching awareness.
This knowledge will serve the further target of building towards an improved protocol for training patients with cerebral blindness to recover part of their lost visual functions.

Study design

Each patient is its own control in a double-training paradigm. Each patient receives two rounds of training.
One training is directed at the hemisphere with the intact visual field (control). The test-training is directed at the field defect.

Each training variant is preceded and followed by a round of dependent measurements that determine
(1) the status of the DEFECTIVE visual field by subjective (perimetry) methods
(2) the status of the DEFECTIVE visual field by objective techniques (fMRI of cortical visual maps , structural MRI of cortico-cortical pathways)
(3) the status of the visuo-behavioural performance in a driving simulator
(4) reading performance

Apart from the training order, there is one further manipulation: the training stimulus. One group of patients receives training with point stimuli. The other group receives training with extended optic flow stimuli that fill the majority of the visual field (diameter: ~ 100 deg). Thus, the 40 patients are randomly allotted to 4 groups according to training order and training stimulus. (the training stimulus is identical for control and test training).

A training effect (for the test- or control training) means the change in the status of each of above mentioned dependent measures (1-4) as determined from a comparison of the pre-training and the post training measurements. An overall training effect (of test / control training irrespective of order) means the change in status of each dependent measure prior to all training and following both training rounds.

Our tests for the effectiveness of the visual-training compare the effects of the test training of the field defect with the effects of the control training of the intact field for each output measure separately.

Finally, to evaluate the Quality of life improvement further each patient participates in three QoL questionnaires and a (G)oal (A)ttainment (S)caling assessment at the start and the end of the study.

Intervention

The training is performed at home with a computer/display system that manages the training (stimuli) and controls the eye fixation by the patient (using a webcam). When the patient breaks fixation the training stimulus is terminated and the trial discounted and repeated later. Patients train 5 days a week for one hour during 16 weeks (8 weeks test-training and 8 weeks control-training).

Most measurements (see section study design) are carried out three times (prior to the first training, in between the two training periods and following the second training). The measurements will be done on three successive days (day 1: MRI; day 2: Behavior/perception; day 3: Behavior/perception). Each test-day comprises on average 2 hours of measurements.

Patients will undergo standard perimetrical tests to map out the visual field. Eye fixation is monitored during perimetry.

Functional and structural MRI measurements are done at the Donders' Centre for Cognitive Neuroimaging in Nijmegen.
During structural MRI the patient is placed in the dark without a task. During fMRI a visual stimulus is presented that activates different parts of the visual field successively. Off-line analysis of the MRI signals allows reconstruction of the retinotopic fields of the occipital and other visually sensitive cortex. One important limitation in many investigations is the limited visual stimulus size that one can offer in the bore of the MRI scanner. We have solved this problem largely by an in-house custom-built projection system that allows stimulation with a diameter of about 120 degrees. This results in a much extended cortical activation region.
We place a projection screen very close (± 3cm) to the eye. Because the naked eye cannot accommodate at this nearby projection surface, the patient needs to wear a soft contactlens of about 30 Diopters in one eye. We provide this contactlens. The other eye is covered. The patient places the contactlens in his/her eye and may ask for assistence from the investigator if need arises. To this end the investigator has received an instruction session from the supplier

(Visser Contact B.V. Nijmegen).

Study burden and risks

In earlier studies we observed that virtually all patients (voluntary applicants) were able to conform to the requested training efforts. This means that the requested regime of a daily 1-hour training for 5 days per week is not an excessive burden. In case that a patient should find one straight hour of training too long, he/she is allowed to train 2 x 30 minutes or 3 x 20 minutes per day.
Perimetry measurements are common practice in opthalmological settings. Both perimetry and head-mounted camera-based eye tracking procedures provide no risk or burden.
The MRI scanner produces a lot of noise, therefore each patient receives earplugs during scanning. As far as is known, there are no risks involved in functional MRI acquisition. Patients are screened for MRI counter indications. If these are absent, MRI scanning is safe.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

PO Box 9101
6500 HB Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

PO Box 9101
6500 HB Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Visual field defect as result of stroke; chronic stroke patients (post onset time > 10 months); age between 18 and 75 years; ability to fixate eyes on a stationary point; capability of sustained concentration to perform training.

Exclusion criteria

visual neglect; MRI contra-indications.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-06-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	27-02-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL38477.091.11