A randomised clinical trial objectively comparing the effect of patching therapy with video gaming for amblyopia

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To achieve a valid comparison of the effect of gaming and patching therapy on visual acuity, with compliance measured electronically.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Vision disorders
Study type	Interventional

Summary

ID

NL-OMON45946

Source
ToetsingOnline

Brief title
Patching or gaming for amblyopiatreatment?

Condition

- Vision disorders

Synonym
Amblyopia, lazy-eye

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: subsidie van stichting Uitzicht;stichting Lijf en Leven;stichting ODAS

Intervention

Keyword: Amblyopia, behavioural training, compliance, fMRI., patching therapy, visual acuity improvement

Outcome measures

Primary outcome

The visual acuity after 24 weeks of patching therapy (actual dose received)

compared to the gaming therapy in adults and children.

Secondary outcome

- The stereoacuity and contrast sensitivity after 24 weeks of patching therapy

(actual dose received) compared to the gaming therapy in adults and children.

- The fMRI changes in the visual cortex after either treatment in the adult

group.

- The quality of life in amblyopia treatment with patching therapy compared to

gaming therapy.

- Investigating information needs for patients to support patient participation

in clinical decision making.

Study description

Background summary

Amblyopia affects 3% of the children and is caused by strabismus (misaligned), anisometropia (unequal refractive error) or both. The standard treatment is glasses and patching therapy preferably before 8 years old. From North-America, behavioural training, i.e. dichoptic training , perceptual learning and video gaming, has become increasingly popular. The rationale behind these games is by using dichoptic stimulation (using both eyes), with the contrast of the stimuli presented to the good eye reduced to match the appearance of the same stimuli when shown to the amblyopic eye, suppression can be alleviated. The many studies now conducted in the USA demonstrate improvement in visual acuity with

the games, the effect however is limited to an average of 1.8 lines, while visual acuity improvement with patching therapy is up 7 lines. Nevertheless, the speed of improvement is markedly quicker with gaming: 17 hours of gaming compared to 142 hours of patching is necessary to achieve one line of visual acuity improvement. In these studies, prescribed patching-time was compared to realised game-time. As we have previously demonstrated the average level of compliance with patching therapy is only 50% and 9% of the children are not patched at all. Because of a patent-issue we can only measure compliance electronically in Europe using the ODM. It seems only logical that we conduct this study in which we compare the effect of both treatments. It would have serious consequences if all newly diagnosed amblyopic children would receive gaming therapy whilst in the studies prescribed patching time was compared to realised game-time. In addition, there is no information available about patient preferences and experiences of video gaming as amblyopia treatment. As video gaming may be a future treatment performed by orthoptics, it is important that orthoptists can inform patients not only about the effect, but also on other aspects of the treatment, such as the impact of the treatment on daily life. Moreover in order to support patient participation in clinical decision-making, we need to know their information needs.

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Study objective

To achieve a valid comparison of the effect of gaming and patching therapy on visual acuity, with compliance measured electronically.

Study design

The study design will be a prospective randomized clinical trial. All newly diagnosed amblyopic children will be recruited (see also study population). After written consent is obtained the participants will be randomized to either the patching or video game treatment by the independent researcher (the PhD student). Both treatments will continue on for 24 weeks.

At the start of the treatment periods and after every two weeks visual acuity, stereo acuity and contrast sensitivity will be assessed by the researcher orthoptist who is blinded as to randomization and treatment. A treatment period of 24 weeks is adopted as the literature has shown that most of the children achieved their best visual acuity with 150 to 250 hours' cumulative dose of patching.The fastest improvement in visual acuity occurred in the first six weeks of patching. For the dichoptic action video game it has been demonstrated (in adults) to show an improvement after 17 hours of training, however participants continued to improve after 26 hours as well. This would involve a schedule of at least one hour of training per week.

In addition together with some basic characteristics a validated questionnaire will be assessed, in order to collect information about the impact of the amblyopia and the treatment on vision-related quality of life. To adult participants, the A&SQ (van de Graaf et al. 2004) will be sent to their home and collected at the first visit at the HU. Children and their parents will be interviewed face to face when they visit the HU following the CVFQ (Felius et al. 2004) clinic and their parents will be asked to fill in the CVFQ (Felius et al. 2004) which will be sent to their home in advance of their visit. Also, the CAT-QoL will be assessed together with eight additional questions.

Treatment:
1) Patching therapy
The non-amblyopic eye will be patched for two hours per day. Compliance with therapy will be monitored with the ODM.

2) Video game
A dichoptic custom-made Unreal Tournament video game was developed by Levi*s group. The game is played under dichoptic viewing conditions in order to reduce suppression and promote fusion, while challenging the amblyopic eye with an embedded perceptual learning task.
The important aspect of this video game is that it presents the same image to each eye (except for Gabor patches and suppression checks) with reduced luminance/contrast in the fellow eye, in an attempt to promote binocular fusion, whereas other dichoptic video game studies have presented different game elements to each eye so that binocular combination is required to play the game.11
There is also a YouTube about the previous version of the game: https://www.youtube.com/watch?v=71RML96XxCI

3) fMRI scans
In collaboration with the Netherlands Institute for Neuroscience in Amsterdam functional magnetic resonance imaging (fMRI) scans will be conducted on 10 adult subjects, prior to the treatment, and after completing the treatment (see Fig. 1). The scans will take place on a 3T scanner.

Functional MRI is a neuroimaging procedure using MRI technology that indirectly measures brain activity by detecting changes associated with blood oxygenation. This measure correlates well with the underlying neuronal activity and has been used in a multitude of studies to further our knowledge of brain function. In this study we are specifically interested in how video-game training / patching affects the basic neural representation of visual stimuli in cortex. We will use both artificial stimuli, such as gratings, which can be well controlled, as well as naturalistic stimuli to study the daily visual experience of the patients. We will examine the fMRI response to stimuli presented to either eye in isolation and the two eyes simultaneously before and after patching therapy / gaming. We are particularly interested in studying at which level in the cortical visual hierarchy therapy induced changes occur. Does video game

training/patching lead to enhancements in low level visual areas only, or are neural representations of visual stimuli in high-level visual areas also affected? To answer this question we will use state-of-the-art multi-voxel pattern classification techniques to *decode* which visual stimulus was presented, and to which eye. As an input to the decoders we will use the fMRI activity patterns from low-level or high-level visual areas. If video-game training / patching leads to strengthened or more reliable neural coding of the stimulus this should lead to better decoding. Furthermore, we aim to link the improvements in decoding accuracy observed in the fMRI experiments with the clinically measured improvements in visual acuity.

4) Qualitative Study
Based on the outcome of the additional questionnaire a heterogenic sample of children and adult participants (i.e. various age, gender, visual acuity, treatment preference etc.) will be selected for an additional interview at the end of both treatments for a more in-depth analyses of their experiences and preferences of the amblyopia treatments. Topics in the interview guide will include the impact of each amblyopia treatment on social and emotional aspects of the child*s life and family life, the impact of the treatment on participation of the child for example at school or daycare and the view of the parents on compliance to the suggested therapy. In addition, information needs form patients to support patient participation in clinical decision making will be investigated. Each interview will be analyzed and based on the results, the interview guide for the next interview will be adapted. More interviews will be planned until the information is only confirmatory.

Intervention

1) Patching therapy
The non-amblyopic eye will be patched two hours per day. Compliance with therapy will be monitored with the ODM.

2) Video game
A dichoptic custom-made Unreal Tournament video game was developed by Levi*s group. The game is played under dichoptic viewing conditions in order to reduce suppression and promote fusion, while challenging the amblyopic eye with an embedded perceptual learning task. See fig 3.

Study burden and risks

By proper extensive screening and (orthoptic) examination of participants there are no potential risks associated with fMRI and the video games. There are no risks in wearing the ODM.

There are no physical or psychological risks involved in the behavioural tasks. The subject is seated comfortably, visual stimuli are presented on a computer

monitor set at a comfortable light level and the button press response requires a minimal amount of effort. Possible fatigue may occur due to the repetitiveness of the task but the subject may discontinue an experimental run at any time and may take breaks between runs.

There are minimal risk associated with playing video games. The frequent use of joystick may cause slight mechanical fatigue: finger irritation from repetitive use of the joystick has been reported in a console player. Participants may develop an interest in video game playing and may continue playing video games after the conclusion of the study on their own time. Since the modified kids friendly game that we have designed does not include any violence, there is no risk which may typically be associated with violent action games. Some participants may experience mild to moderate nausea as a result of the virtual motion associated with action game play. Nausea usually subsides after the first few training sessions and participants who do not feel well are permitted to end a session early and make up training time later.

Numerous studies have demonstrated a positive effect of gaming on visual acuity improvement. Thereby, the speed of the improvement is markedly quicker with gaming compared to patching therapy. The main issue these studies is that compliance in patching therapy is not measured electronically, thus objectively. It would have serious consequences if all newly diagnosed amblyopic children would receive gaming therapy whilst in the studies prescribed patching time was compared to realised game-time.

Our study will be the first study to compare the effect of patching therapy, using the ODM to objectively measure compliance, with the effect of a novel dichoptic action video game in children as well as in adults. In addition, the adult participants will undergo fMRI scans to document any changes in the visual cortex before and after either therapy. This study will first provide evidence on the speed of visual acuity improvement comparing both treatments, and then shed further light on the plasticity of the brain in adults.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Children: Newly diagnosed amblyopia; i.e. never had treatment for amblyopia before with an interocular difference in visual acuity of at least 0.2 logMAR.;Adults: The adult population will be recruited from a previous prospective randomised controlled trial conducted in the Hague in 2001 (MEC-2015-482). In case the amblyopia still persists; i.e. visual acuity difference 0.2 LogMAR lines

Exclusion criteria

Children: Previous amblyopia treatment, a non-comitant or large angle constant strabismus >30Prism dioptres, a neurological disorder, nystagmus, other eye disorders and diminished acuity due to medication, brain damage or trauma.;Adults: a non-comitant or large angle constant strabismus >30Prism Dioptres, a neurological disorder, nystagmus, other eye disorders and diminished acuity due to medication, brain damage or trauma, participants with medical devices or implants that are not certified as MRI-compatible.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-12-2017
Enrollment:	124
Type:	Actual

Ethics review

Approved WMO Date:	12-04-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL57506.078.16