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Virtual reality social prediction training for pediatric patients with cerebellar diseases

Submission date
12/01/2018

Recruitment status
No longer recruiting

Registration date
12/03/2018

Overall study status
Completed

Last Edited
07/05/2024

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English Summary
Background and study aims
In the last 20 years, parts of the brain that were traditionally thought to be involved in motor control, particularly the cerebellum, have been recognized as also having an important role in cognitive, social and affective domains. Children and adolescents with diseases affecting these parts of the brain (e.g., congenital or acquired cerebellar alterations) have problems with movement and also social cognition. Rehabilitation should therefore not only involve the recovery of motor function but also of higher-order abilities, such as processing of social stimuli. In this study a Virtual Reality (VR) environment is used to test a brand-new social skills intensive training specifically tailored to improve predictive abilities in social scenarios. The GRAIL is an integrated platform that allows patients to move in natural and attractive VR environments, providing sophisticated sensory information to users. Increasingly demanding social situations are simulated that require the attribution of mental states (e.g., preferences) to other individuals in order to predict their behavior. The aim of this study is to investigate the feasibility and effectiveness of an intensive VR social prediction training protocol (VR SPIRIT) in Italian pediatric patients with cerebellar injury, both congenital (present from birth) and acquired.

Who can participate?
Children and adolescents aged 7-25 with congenital (i.e., Joubert syndrome, cerebellar hypoplasia etc) or acquired cerebellar diseases with an IQ greater than 45, with no important behavioral problems and with no severe sensory and/or motor deficits that may prevent the use of the Motek VR technology

What does the study involve?
Participants are randomly allocated to one of two groups. Group 1 receives the social prediction VR training for two weeks (four daily sessions in a week). In each 1-hour session, 80 trials of the experimental program and one of four games available in the GRAIL kit are used. For each weekly session, a different game is played in a random order. Group 2 receives a control VR training of the same duration (two weeks, four 1-hour sessions per week) as the experimental training which consists of, for each session, a pathway search game and the same four games from the Motek kit, but not the social prediction experimental program. Participants are

evaluated before and after the training using the same type of VR experimental program in a different scenario. Furthermore, a series of tests and questionnaires are completed before and after the training and in a follow-up session.

What are the possible benefits and risks of participating?
Benefits are expected in social prediction abilities, and consequently in social skills. Improvements are presumed to occur in cognitive domains indirectly engaged in the training (attention and executive functions, memory, visuospatial abilities, sensorimotor integration) and in general implicit learning as well as quality of life. No risks are expected. Excluding the presence of severe sensorimotor or behavioral disorders, which could compromise the use of GRAIL technology, prevents any risks of taking part in the training.

Where is the study run from?
Child Neuropsychiatry and Neurorehabilitation Unit of the Scientific Institute IRCCS E. Medea – Bosisio Parini (Lecco) (Italy)

When is the study starting and how long is it expected to run for?
February 2018 to January 2022

Who is funding the study?
Italian Ministry of Health (Italy)

Who is the main contact?
Dr Renato Borgatti

Contact information

Type(s)
Scientific

Contact name
Dr Renato Borgatti

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NET-2013-02356160-4

Study information

Scientific Title
Virtual Reality Social Prediction Improvement and Rehabilitation Intensive Training (VR SPIRIT) for pediatric patients with cerebellar diseases

Acronym
VR SPIRIT

Study hypothesis
Current hypothesis as of 20/12/2018:
The aim is to investigate the feasibility and efficacy of a new intensive cognitive rehabilitation protocol in a sample of Italian patients aged 7-25 with congenital or acquired cerebellar diseases. For what concerns the efficacy, the aim is to estimate improvement outcomes in social prediction ability. The hypothesis is that the VR rehabilitation protocol could:
1. Enhance social prediction ability resulting in a better understanding of other people's intentions and behaviors
2. Facilitate general-domain implicit learning ability
3. Indirectly improve cognitive performance in specific domains (attention and executive functions, memory, visuospatial abilities, sensorimotor integration)
4. Reinforce the effects of other specific-domain cognitive trainings administered in Institute (e. g., home-based computerized cognitive training)
5. Produce an amelioration of patients' quality of life

Previous hypothesis:
The aim is to investigate the feasibility and efficacy of a new intensive cognitive rehabilitation protocol in a sample of Italian patients aged 8-16 with congenital or acquired cerebellar diseases. For what concerns the efficacy, the aim is to estimate improvement outcomes in social prediction ability. The hypothesis is that the VR rehabilitation protocol could:
1. Enhance social prediction ability resulting in a better understanding of other people's intentions and behaviors
2. Facilitate general-domain implicit learning ability
3. Indirectly improve cognitive performance in specific domains (attention and executive functions, memory, visuospatial abilities, sensorimotor integration)
4. Reinforce the effects of other specific-domain cognitive trainings administered in Institute (e. g., home-based computerized cognitive training)
5. Produce an amelioration of patients' quality of life

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Scientific Institute (IRCCS) Eugenio Medea, 01/03/2016, ref: #284 Rev. 1

Study design
Single-center randomised active controlled clinical trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Condition
Congenital or acquired brain injury

Interventions
The study applies a randomized controlled trial design, randomly assigning patients to one of two groups undergoing two different rehabilitation programs: Group 1 receives the social prediction VR training for two weeks (four daily sessions in a week). In each 1-hour session, eighty trials of the experimental program and one of four games available in the GRAIL kit are administered. For each weekly session a different game is administered in random order. Group 2 receives a control VR training of the same duration (two weeks, four 1-hour sessions per week) as the experimental training which involves, for each session, a pathway search game and the same four games from the GRAIL kit, but not the social prediction experimental program. Pre- (T0) and post-training (T1) evaluation sessions, using the same paradigm of VR experimental program in a different scenario, are administered to both groups. Furthermore, a series of neuropsychological test and clinical questionnaires are administered at T0 and T1 and in a follow-up evaluation session (T2).

Before the training (T0), a battery of neurocognitive tests (NEPSY-II) spanning different domains, and specifically social perception abilities, are administered to all participants. Both groups also receive a 10-minute training of how to move with Grail technology using the “path” scenario. Then, a pre-training evaluation through a VR game session, based on the same paradigm of the experimental training but a different scenario (“sweet stands”), and a computer-based Action prediction task are administered. Moreover, at T0, both patients and parents compile questionnaires on quality of life (TACQOL) and parents even complete the Child behavior Check List (CBCL). In order to verify and compare the effects of the experimental protocol and of the Motek games sessions, at the end of the two-weeks training (T1) all participants are re-evaluated with the same neurocognitive tests, the VR evaluation scenario and the Action prediction task. With the aim to investigate the far transferability of the effects, a follow-up evaluation is provided after two months (T2). Specifically, participants are tested with the same neurocognitive battery, the Action prediction task , the self- and parent-compiled TACQOL and the CBCL parent-version.

The rehabilitation training is administered in the Grail Lab of the E. Medea Scientific Institute that allows the participants to move in an immersive VR environment. Two different settings have been developed specifically for this study: the “playground” scenario for the social prediction training and the “sweet stands” one for the pre and one for the post-training evaluations. In both scenarios, three objects are located in a semicircle with the same distance from the starting point; for the “playground” setting there is a swing, a circular carousel and a rocking carousel, while in the “town square fest” setting there is an icecream, a donut and a

lollipop stand. In each trial, an avatar moves from the starting point to one of the objects. Four different avatars are available, balanced for gender and clearly identifiable by typical features (hair and t-shirt color). Each avatar moves toward one of the objects with pre-established probability.

Considering twenty trials per avatar, eighty trials are administered in each session. Within a session, events take place in a pseudorandom way in respect to the pre-established probabilities.

With the aim to balance the association between avatars and objects, four diverse sessions (A, B, C, D) were obtained, in which the avatars' probability of moving toward a specific objects is equally distributed. The four sessions are randomly administered during the first week and repeated in the same order in the second week. The two evaluation sessions at T0 and T1 are randomized in order to avoid repetition of the same events (e.g, for patient 1 session A at T0 and session B at T1, for patient 2 session B at T0 and session A at T1 ecc).

At the beginning of each session, participants are asked to move toward the object chosen by the avatar and activate it before him/her. The avatar, one per trial, moves towards an object, reaching it in ten seconds. The path is not rectilinear: first, it is a straight-line trajectory and then, three-quarters way through, it splits into three ways. Thus, participants are not exposed to motion cues concerning avatars' directions until the crossroad. In the linear part, participants can pass the avatars, while after the division the maximum speed of the avatars is the same as patients, so that avatars cannot be surpassed. As a result, participants are forced to move according to the predicted avatars' behavior. When the participant reaches one of the objects, the object is activated providing a visual reinforcement, while the trial is interrupted after five seconds when the avatar reaches the objects and patients are invited to try again. The object reached by the avatar is always visible to the participant, for both successful and unsuccessful trials, in order to provide information on the avatar's preferences to be used in the next trial. Furthermore, when the participant anticipates the avatar in reaching the chosen object, thus predicting avatars' intentions, he/she, in addition to visual reinforcement (activation of the object), also receives an auditory reinforcement (clapping sound), which signals the scoring of a point in the game.
In each session, G1 completes eighty social prediction trials and then plays one of four selected games from the GRAIL kit. Differently, G2 is exposed for the same amount of time (1-hour session per day, four sessions per week for two weeks) to sessions in which participants play the 10-minutes "path" scenario and all of the four selected GRAIL games. The four selected games are "skiing", "balloon shooting", "world soccer" and "traffic jam". These games have been chosen because they do not present social agents and do not require any form of prediction ability. In the "skiing" game participants have to do a slalom between snowmen, scoring a point when they pass each snowman on the right side. In the "world soccer" one, children kick a virtual ball toward a goal: they score points when they hit targets put inside the goal. In the "balloon shooting" game, participants have to hit balloons appearing in a natural environment simply by pointing at them. In the "traffic jam" game, participants are in the middle of a crossroad and they have to raise the left or right foot according to the cars' movements.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

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Primary outcome measure

Training feasibility, assessed using:
1. Number of dropouts: number of children who renounce to complete the two-weeks training
2. Number of sessions completed per child: total number of sessions done in front of the total number proposed of eight sessions. Timepoint: two weeks (T1-after training conclusion)

Training acceptability, assessed using:
1. Acceptability questionnaire: an ad hoc questionnaire completed by participants and another one by their parents after training conclusion to assess subjective evaluation of training accessibility and efficacy. Timepoint: two weeks (T1-after training conclusion)

Primary outcome measure:
1. Participants' performance during the VR social prediction training (scores in each session, duration per trial, mean speed); Timepoints: daily during the training
2. Social prediction ability: performance during the pre and post-training evaluation in the “sweet stands” scenario; Timepoints: measured at baseline (T0) and two weeks (T1-after training conclusion); accuracy and reaction time in the testing phase of a validated PC-based Action prediction task (Amoruso et al., 2016). Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)

Secondary outcome measures

1. Social cognition: Theory of mind Part A and B and Emotion recognition of NEPSY-II testing battery (Korkman et al., 2011). Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
2. Implicit learning: accuracy and reaction time in the familiarization phase of an Action prediction task (Amoruso et al., 2016). Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
3. Executive functions (inhibition and flexibility): Inhibition test of NEPSY-II. Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
4. Visual attention: Visual attention test of NEPSY-II. Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
5. Visuospatial and visual-perceptual abilities: Geometric Puzzle and Picture Puzzle tests of NEPSY-II. Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up).
6. Memory: Memory for drawings test of NEPSY-II. Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
7. Sensorimotor functions: Fingers-tapping test of NEPSY-II. Timepoints: measured at baseline (T0); two weeks (T1-after training conclusion); two months (T2-follow-up)
8. Behavioral problems: CBCL 6-18, Parent version (Achenbach & Rescorla, 2001; http://www.aseba.org). Timepoints: measured at baseline (T0); two months (T2-follow-up)
9. Overall functioning and quality of life assessed using the TACQOL (TNO Quality of life / LUMC, 2001) that assess quality of life, health and well-being of patients in several areas. This questionnaire is presented in two forms: the self-compiled and the parent-compiled one. Timepoints: measured at baseline (T0); two months (T2-follow-up)

Overall study start date

01/02/2018

Overall study end date

28/01/2022

Eligibility

Participant inclusion criteria
Current inclusion criteria as of 20/12/2018:
Children, adolescents and young adults (aged between 7 and 25 and IQ >45) with a congenital or acquired cerebellar disease who had been referred to the Child Neuropsychiatry and Neurorehabilitation Unit of the Scientific Institute IRCCS E. Medea in the last years

Previous inclusion criteria:
Children and adolescents (aged between 8 and 16 and IQ >60) with a congenital or acquired cerebellar disease who had been referred to the Child Neuropsychiatry and Neurorehabilitation Unit of the Scientific Institute IRCCS E. Medea in the last years

Participant type(s)
Patient

Age group
Child

Lower age limit
7 Years

Upper age limit
25 Years

Sex
Both

Target number of participants
A final sample of 21 patients per group has been set for such a study in order to detect a between-group difference (independent sample t-test, two tailed) between the effects of the experimental vs. control training (T1-T0) of moderate effect size (Cohen's d = 0.8) with a power of 0.80 and alfa level set at $p < 0.05$. The software G Power 3 was used for this estimation.

Total final enrolment
28

Participant exclusion criteria
1. Severe sensorial, motor and/or behavioral problems that could interfere with the use of Grail technology
2. Being simultaneously involved in a different cognitive rehabilitation treatment, to avoid excessive demands to children and possible interference on training adherence rates
3. Having been involved in a different cognitive rehabilitation treatment in the last six months before training, to avoid confounding follow-up effects

Recruitment start date
01/02/2018

Recruitment end date
31/12/2021

Locations

Countries of recruitment
Italy

Study participating centre
Scientific Institute IRCCS Eugenio Medea
Via Don Luigi Monza 20
Bosisio Parini (Lecco)
Italy
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Sponsor information

Organisation
Scientific Institute (IRCCS) Eugenio Medea

Sponsor details
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Sponsor type
Research organisation

Website
http://www.emedea.it

ROR
https://ror.org/05ynr3m75

Funder(s)

Funder type
Government

Funder Name

Ministero della Salute

Alternative Name(s)
Italian Ministry of Health, Italy Ministry of Health, Ministry of Health of Italy, Ministry of Health - Italy, Ministry of Health, Italy

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Italy

Results and Publications

Publication and dissemination plan
The protocol will be published before patient recruitment. The results on feasibility and efficacy will be published in international peer-reviewed journals. The trialists intend to publish the preliminary data on feasibility within 6 months and the preliminary data on efficacy after 1 year. Final efficacy results will be published within 6 months after the end of the training.

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Renato Borgatti. Data are collected in a protected database and are anonymized, as a research member assigns to each participant an identity number that substitutes the name. Participants' parents give written informed consent to anonymized data use. Preliminary data on feasibility and efficacy will become available from December 2018. All data will be available for five years after the relevant publication. All materials and methods regarding data collection and treatment have been analyzed and approved by the Ethics Committee of Scientific Institute (IRCCS) Eugenio Medea and all procedures are in agreement with the principles expressed in the Declaration of Helsinki.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	14/01/2020	16/01/2020	Yes	No
Basic results		23/02/2023	24/02/2023	No	No
Interim results article	Preliminary data on efficacy	01/11/2021	24/02/2023	Yes	No
Results article		03/05/2024	07/05/2024	Yes	No