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Emanuele Maria Merlo
University of Messina, Department of Adult and Childhood Human Pathology "Gaetano Barresi", Messina, Italy, emerlo@unime.it

Liam Alexander MacKenzie Myles
University of Cambridge, Department of Psychology, Cambridge, UK

Salvatore Marco Pappalardo
Software Engineering Italia S.R.L., Piazza Abramo Lincoln 7, Catania, Italy

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The VESPA Project: Virtual Reality Interventions for Neurocognitive and Developmental Disorders

Emanuele Maria Merlo[1,2*], Liam Alexander MacKenzie Myles[3], Salvatore Marco Pappalardo[1]

[1]Software Engineering Italia S.r.l., Piazza Abramo Lincoln 7, Catania, Italy
[2]University of Messina, Department of Adult and Childhood Human Pathology "Gaetano Barresi", Messina, Italy
[3]University of Cambridge, Department of Psychology, Cambridge, UK

ABSTRACT

VESPA is a financed project supported by the Sicilian Regional Research and Development funds, and it is structured by the development, research and validation of Virtual Reality (VR) based application for the diagnosis and treatment of neurocognitive conditions. In particular, this article presents its characteristics, referred to as the first (2013-2015) and second (2021-ongoing) generations of VESPA, with particular reference to literature regarding the VR technology application and development, the VR treatment of neurocognitive conditions and prior versions of this intervention.
Through a comprehensive review of the research conducted over the last 5 years, evidence has emerged supporting VESPA's aim and scopes, highlighting how the application of VR can be considered to add value to typical rehabilitation/therapeutic paths. VESPA project generations are then presented in detail, including specific session/task battery characteristics, 2.5D, 3D and 5D typologies, system usability and architecture and pathological domain-based dynamics and features. The discussion about VESPA will highlight the current advantages along with limitations and future directions.

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***Corresponding author:**
Emanuele Maria Merlo,
University of Messina, Department of Adult and Childhood Human Pathology "Gaetano Barresi", SwingIt, Catania, Italy
E-mail: emerlo@unime.it

Introduction

With reference to the origin of VR, the phrase Virtual Reality was coined in 1989 (by Jaron Lanier), in the field of computer sciences. The phrase was related to the foundation VPL Research (Virtual Programming Languages) as the first foundation in the field of VR technologies and contents. In line with several studies in the literature, the use of Virtual Reality (VR) in the diagnosis and treatment of various neurocognitive conditions is becoming increasingly important [1-6].

Evidence adheres to several domains, such as in the case of cognitive deficits linked to developmental disorders and diseases [7,8], psychiatric conditions [9-16] and neurocognitive disorders [17-23].

The use of virtual reality to support people with mental health difficulties such as psychosis is well-supported in the literature [24], and our intent is to extend this aim to cross-aboard phenomena in clinical practice and facilitate access to virtual reality. As suggested by Valmaggia, the use of virtual reality has been extended to several mental health problems [25].

In these types of studies, participants enter a virtual environment, like a means of public transportation or a café, populated by avatars who exhibit behaviors which can be interpreted as ambiguous; for example, avatars may be looking at the participant or they may be looking away. An Avatar can be described as a graphical representation of a user, both in anthropomorphic and properly human form [26]. The occurrence of paranoid ideation or hallucinations triggered during the virtual reality experience is then assessed.

The multidisciplinary approach meets the needs and uses of knowledge in the fields of mental functioning, be it typical or abnormal. The key to understanding the phenomena lies in the dimensionality of psychic manifestations and in their quality. It is therefore a question of phenomena, whether they are observed in terms of either descriptive or interpretative models. Therefore, these models allow us to gain knowledge respectively from the intersubjective

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presence of the phenomenon and from its transversal manifestations, as well as from subjectivity aspects.

Discussion

1. Background and application

1.1 Virtual reality and neurocognitive disorders

In the field of neurocognitive disorders, it was demonstrated that VR is a reference point in terms of diagnosis and treatment of related phenomena, as in the field of narrative identity [27], embodied cognition [28-30], spatial, temporal and personal orientation [31-36] and the early manifestations of Mild Cognitive Impairment [37].

With reference to diagnosis and screening, VR tools appeared to be helpful in the emergence of classical phenomena and more specifically in identifying differential manifestations useful for the diagnosis of specific diseases and conditions [38-40].

These data can be extended to prevention, the early manifestations and presentation [41-43], the decision processes about better treatment solutions (e.g. through specific tasks related to certain deficient functions) [44-46], and directly to specific rehabilitation/treatment practices, as suggested by recent high level and quality reviews [47-51].

1.2 Virtual reality and specific diagnostic domains

With reference to Alzheimer's Disease (AD), a recent structured review on technological solutions for the diagnosis and treatment of dementia highlighted that recent technological advances provide potential for the design of innovative methods useful for the assessment, control and management of specific AD manifestations [18]. As suggested by the authors, with reference to previous published research, symptomatic manifestations resulting in the presence of plaques of β-amyloid peptide and neurofibrillary tangles of phosphorylated tau represent phenomena of distinctive proteins for the condition [52].

The innovations applicable to the AD condition refer to the diagnosis [35,53-57], behavioral support [58-60] and treatment [61-63] of the presented symptoms in specific terms.

Parkinson's Disease (PD) can be considered one of the age-related neurodegenerative diseases; its frequency increases with aging [64]. As reported by Poewe et al. [65], about 2-3% of the people over 65 years old worldwide suffer from PD. The condition is characterized by the presence and the occurrence of Lewy bodies (LBs) as abnormal aggregation and accumulation of alpha-synuclein (αSN) in neurons [66,67]. Researchers, as for example Sahihi, Gaci & Navizet [64], highlighted the possibility of implementing VR solutions in order to detect specific PD manifestations, as in the case of alpha-synuclein fibrillogenesis inhibitor. Others referred directly to telemedicine [68], but not directly to VR.

A recent systematic review and meta-analysis on the effects of VR on MCI and dementia suggested the importance of non-pharmacological interventions, with particular reference to significant improvements in cognitive and motor functions of older adults suffering from MCI or dementia [69].

With direct reference to PD, it was demonstrated that VR achieved the same effects of conventional rehabilitation practices and promoted the improvement of performances in patients with Parkinson's Disease [69-71]. In general terms, further studies are needed in order to reach relevant objectives and levels of knowledge occurring with AD.

Multiple Sclerosis (MS) represents an inflammatory disease mostly related to brain and spinal cord myelin sheath damage [72,73]. The impairment related to damage can involve different functions, as in the case of communication and physical-motor abilities [74]. With reference to the application of VR in the treatment of MS, a lack of research emerges through principal scientific research engines. The application of VR for MS has been considered by Rezaee & Zolfaghari with reference to stress levels related to VR exposure [73].

A recent contribution by Kalron and colleagues considered the effect of tele-rehabilitation through VR in patients with MS [75]. The study highlighted the possibility to structure efficient interventions compared to classical rehab programs, in order to verify significance. In 2014, Lonzano-Quilis et al. published a study involving MS patients in VR rehabilitation exploiting a Kinect-based system [76]. Their results suggest that VR treatments can be considered a valid and alternative rehabilitation path to classical ones.

In the light of the evidence emerging through rigorous studies [77], research considered that the involvement of subjects with MS in clinical trials and protocols is useful for the emergence of significance [78-82].

With reference to Intellectual Disability (ID) and Communication Disorders (CD), some of the basic needs referring to the use of VR, within these two domains, were highlighted by Gybas, Kostolányová & Klubal [83]. The authors suggested the possibility of using Augmented Reality (AR) to support people with special educational needs, with a reduced influence of burden related to graphomotorism and cognitive stress, in line with other studies fully centered on stress assessment [84].

ID entails notable cognitive deficits, as measured through standardised intelligence measures [85].

Fu et al. [86] experimented a game-system basis for the rehabilitation of subjects with ID, a system based on Kinect to improve self-care, mobility, and social functions of children. Other older studies [87,88] introduced the use of VR for the above-mentioned domains, with major reference to developmental and intellectual disability, showing good results, also in terms of diagnosis [89].

In terms of effectiveness and results linked to the application of VR with neurodevelopmental realities, recent contributions have confirmed the need for the implementation of clinical-rehabilitative systems [90-94]. In their recent contribution, Jdaitawi & Kan'an published a review regarding the last decade of research on the effectiveness of these methods on people with ID in higher education systems, showing evidence of effectiveness and usability [95].

With reference to Communication Disorders (CD; Communication and Other Neurodevelopmental Disorders), specifically Language Disorder, Speech Sound Disorder, Childhood-Onset Fluency Disorder (Stuttering), Social (Pragmatic) Communication Disorder, and Unspecified, Communication Disorder (considering DSM-5 nomenclature), most of the studies considered these conditions in the light of autistic spectrum disorders and neurodevelopmental conditions, considering the use of VR [90,96]. In particular, through a recent comprehensive meta-analysis [96], the authors described the application of VR as highly recommended. In line with these results and statements, Vasudevan and colleagues highlighted the important role of VR in the treatment of CD [97].

Moreover, a recent review on the use of VR technologies in the field of CD promoted the use of VR with reference to the extensibility of virtual environment to real life experience [98]. The recommendation is linked to the involvement of various figures referring to different fields, in the light of a multidisciplinary approach, in order to guarantee covering all clinical and scientific domains.

In the light of the above-mentioned studies and domains, the aim of this study is to present the VESPA project, considering its first and second generation, including specific information related to its scopes, structure and general articulation.

2. VESPA project - Virtual Environment for Superior neuro-Psychiatry

2.1 Specification and application of VR in the clinical fields

The main objective of VESPA is the development and validation of a highly immersive VR system useful in the diagnosis and treatment of neuropsychiatric conditions. The objective can be considered directly linked to the needs for detection and variation of dysfunctional pathological manifestation, in this specific case, through VR instead of classical implemented methodologies. In these terms, VESPA represents a project providing innovative technologies for different neurocognitive conditions.

The reference is linked to a set of technologies directed to people's interaction with 3D computer databases, involving real time human senses, cognition and abilities. VR can in fact provide credible/realistic experiences in a specific virtual environment, through interaction involving subjects and objects properly referring to the built environment.

The VESPA project is linked to DECIDE (Diagnostic Enhancement of Confidence by an International Distributed Environment, 2010-12 (https://www.eu-decide.eu), whose services enable access to the data produced by means of clinical practices.

Validation is meant to be performed in accordance with the cross-validation definition, so in line with the admitted experimental methods considering conformity objectives of included instrument-tools. This process involves previously validated methods and instruments, along with innovative solutions. In these terms, VESPA will undergo experimentation and validation together with classically used (and validated) solutions, in order to compare results and consider significance represented by a certain acceptable error threshold.

Due imagine realism consists in offering the subject a realistic perception of the objects involved in the virtual environment. VR is highly influenced by concepts such as realism, interaction and immersion, meant as the possibility of creating a sense of sensory isolation and absorption in the environment.

The three main classification types of immersion are:

-First degree, in which the subject can perceive his presence within the environment where he is “immersed”;

-Second degree, in which the subject is able to navigate within the environment;

-Third degree, in which the subject can control exercise over the environment through the user.

First and second degrees are based on graphics and audio simulations, so that the subject is exposed to visual and auditory stimuli, as passive degrees of immersion. The last degree is non-passive, so that the subject is exposed to the proper interaction with objects and virtual environments.

For psychodiagnostic and rehabilitation practices, du Sert et al. define the therapeutic results obtained with Immersive VR and psychological therapies based on current technology, in therapeutic and research terms as encouraging, based on the evidence produced [99].

The inseparability of mental health difficulties from environmental contexts justifies the immersive settings and the virtual involvements of the subjects [100]. The computerized reproduction of interactive environments would allow the treatment of problems linked to specific environmental situations and scenarios, thus reducing the need for laboratories for which it is difficult to reproduce specific contexts and settings and attributable to dysfunctional responses to activating stimuli. This would allow a reduction of the environmental constitution problems and the consequent trigger stimuli, creating a plastic and variable structuring of the experimental and treatment conditions [101]. VR is therefore configured to be useful in the assessment and treatment of disorders, ranging from neurocognitive deficits to relevant clinical symptoms [24].

Assessment, treatment and rehabilitation are keywords in the use of VR in clinical conditions, with high potential in terms of strategic value. The patients' attitudes and the positive responses to methodologies are qualitatively positive, starting from neurocognitive deficient realities, up to psychotic states [24]. The encouraging results require comparison and experimentation. This proposal takes into account the need for experimentation and consideration of any limitations, as well as overcoming by experimentation.

The added value is configured with respect to its adherence to the needs of the NHS, local governments, families and patients. The proposal is therefore in line with the achievement of specific objectives that facilitate the NHS for specific needs. Development and application would produce an increase in the provisioning of care for patients and families [102,103]. The outcomes would consist in a significant decrease in waiting times, in the phenomena of postponement of treatment and treatment drop-out. The dynamics of data acquisition and analysis would be attributable to automated processes, allowing for a reduction in observation and reporting times as well as errors and enabling the possibility of producing standardized evidence. Regarding the reductions in timing, shareability, flexibility in obtaining evidence and replicability represent strength points, considering the multidisciplinary, specifically of a cognitive, affective, psychodynamic, psychophysiological and neurobiological type.

An innovative approach to the problem of cognitive disability is thus manifested, no longer aimed at automatic hospitalization, institutionalization or tracing parallel or special paths, but aimed at building a network of support and opportunities for the patient and his family, at implementing and facilitating cognitive rehabilitation practices.

As reported on the official website, the VESPA System allows a multitude of children and elderly to carry out their daily cognitive-motor rehabilitation directly in schools or in residential facilities, thus ensuring the continuity of school education and assistance and, eventually, solving the problem for care-givers when it comes to picking up and bringing their children to school or to residential facilities after taking them to the headquarters of cognitive-motor rehabilitation.

The VESPA System is a worldwide unique state-of-art system for the evaluation and rehabilitation of cognitive-motor functions (3D visual-spatial abilities, 3D visual and spatial attention, verbal and spatial memory, executive functions, abstract thinking, etc.) through immersive virtual reality. Furthermore, it offers the possibility to specialized staff to supervise the procedure during a videoconference (tele-supervision) (https://www.swing-it.net/progetti/progetto-vespa/?lang=en).

2.2 Virtual Environment for a Superior neuro-PsychiAtry 1st Generation

The first generation of VESPA began in 2013 (ended December 2015) and it was financed by the Sicilian Regional Research and Development funds and structured by development, research and validation intents. In particular, the first generation of VESPA referred both to developmental and adult domains. The involved diagnostic fields referred respectively to Alzheimer's Disease for adults, Intellectual Disability and Linguistic Disorders for developmental domains.

With reference to AD, the structure of the project's tools was meant to organize rehabilitative paths through a battery of tasks, to be organized in series. The specific tasks provided for parameters and metrics strictly related to the patients' performances. With reference to parameters, they were established in terms of input/settings useful for the carrying out of the tasks. Metrics referred to the function performance, with direct reference to cognitive functions.

The course of each task was structured with direct reference to deficient functions, detected through psychodiagnostic instruments. The protocols which referred to both adults and subjects at the age of development and to clinically admittable patients (the inclusion criteria), were structured as follows:

- The neuropsychological test administration (A - baseline, e.g. prior to the assessment);
- The administration of the VESPA tasks (B treatment, organized in sessions)
- The neuropsychological test administration (A'- e.g. - post assessment)

Batteries for adults were set to be tasks involving patients in interaction with objects, therefore subjected to a number of repetitions. The interactions were carried out within a setting in which the subject can manipulate, arrange, order the objects following the instructions. Other batteries were supported by internal questionnaires properly based on personal, temporal and spatial orientation together with sociodemographic data.

Batteries for developmental age children and adolescents were based on basic interactions, communication, repetition and manipulation of specific "objects" meant as proper everyday life objects and language units.

With direct reference to psycholinguistic tasks, the battery appears to be developed in order to treat disorders of the expressive/linguistic area through interactions based on instructions. Manipulation and responses to linguistic units were based on correspondence, comparison, properties, which the subject will encounter in repeatable events.

The battery appeared to be calibrated in order to produce interactions within established scenarios, with objects and repeatable events depending on the clinical dispositions (number of events). The tasks include structures that adhere to the clinical needs, resulting from the state of art. The interactions were carried out within a setting where the subject could manipulate/arrange/order the objects following the instructions.

2.3 Virtual Environment for a Superior neuro-PsychiAtry 2nd Generation

The second generation of VESPA started in January 2021 (being still ongoing) and provided the inclusion of other diagnostic domains. Multiple Sclerosis and Parkinson's Disease have been included with reference to adult rehabilitation task batteries. Considering developmental age, more specific definitions of Communication Disorders and Intellectual Disability were provided.

As in the case of first-generation VESPA, validation protocols were maintained:

- The neuropsychological test administration (A - baseline, e.g. prior to the assessment);
- The administration of VESPA tasks (B treatment, organized in sessions)
- The neuropsychological test administration (A'- e.g. post assessment)

With reference to AD, the first-generation VESPA task batteries were preserved, despite being implemented and better defined for both new technological improvements and more detailed clinical specifications (such as better expressed/implemented parameters and metrics results). Starting from the adult domain, two new batteries were projected and developed.

In particular, the newly introduced Cog task set refers to the rehabilitation of cognitive functions in adults, by extension and with reference to the additional diagnostic domains provided for in second generation VESPA (Multiple Sclerosis and Parkinson's Disease).

The new tasks account for the interaction of the subject within certain scenarios, referable to the manipulation and use of objects, with repeatable sessions as determined by the assistance of clinical operators. In line with some of first-generation VESPA tasks, the inspiration of the new tasks involved experiences, situations and settings related to everyday life dynamics, in order to implement the cognitively determined interactions of the subjects who foresee deficits.

For the developmental age, the newly introduced task set, through the introduction of fine detections, as in the case of tracking, accounts for the innovative rehabilitation activities through the understanding and metric calculation normally suggestive in classical clinical/ rehabilitation practice.

Taking into account the age and specific deficits, the tasks account for the interaction of subjects within a given space, with the aid of manipulable/ placeable/ categorizable objects, for repeatable sessions. Taking into account the clinical target, the activities are inspired by the need to maintain a tendentially ludic character.

A particular added value referred to the administration of olfactory stimuli, in the gaseous state, for the involvement of the subjects in terms of sensory application, together with the dynamic movement platform, useful in order to allow movements in different spatial directions, such as full 5D.

VESPA 2 will drive the VESPA system to TRL 7 (the full prototype operation). The project will run clinical studies and trials in order to validate the current system architecture in terms of efficacy in service provision to end-users (patients). This will complete the definition of the system crosschecking psychiatrist requirements and provide guidelines towards the official approval of the Ministry of Health as medical devices.

2.3.1 VESPA System Infrastructure and IT Services

In Europe, the National Health Services foster an innovative approach to cognitive disabilities aimed at building a support network making cognitive rehabilitation easier and producing social integration, seeking for a more effective deployment of resources towards the growth of rehabilitation capabilities addressing a daily increasing demand. The adoption of such a pioneeristic approach moves through the implementation of diagnostic and rehabilitation services available not only in hospitals but also in schools (e.g. ID and CD), specialized structures and retirement homes (AD, PD, MS). Ideally, in order to decrease the costs, cognitive-motor rehabilitation provided outside the hospitals should take place through video-conferences or tele-supervision.

A fully immersive Virtual Reality computerized system such as VESPA, which is remotely tele-supervised by clinical personnel located in control centers, fully comply with the approach described above. This system provides quantitative and qualitative evaluation of motor-cognitive functions enabling fast and easy diagnosis or treatment. The VESPA system will allow numbers of young and elderly people to live their own daily rehabilitation paths not only in dedicated clinical centers, but also in schools, retirement homes, and (why not?) usually frequented everyday places. Continuity in education and assistance will be easily ensured, while parents and caregivers will not be requested to provide transportation to rehabilitation centers anymore. The system also promises to make results as effective as classical diagnostic and rehabilitation processes in a shorter period of time. This makes neurocognitive condition management faster and faster will also be the treatment. This allows subjects to improve learning curves and better exercise cognitive functions, and produces a decrease in the impairment effects in elders suffering for dementia and other neurodegenerative diseases.

Thus, pathologies such as AD, PD and MS require advanced diagnosis through the evaluation of structural markers by means of neuroimaging techniques requiring huge computing and storage resources [104-107] as well as a large amount of reference data from healthy individuals; the integration of DECIDE services in VESPA enables access to reference distributing data-banks and elaborating electroencephalography (EEG), magnetic resonance imaging (MRI) and Positron Emission tomography (PET) for diagnosis.

To this aim, the 1st and 2nd generation VESPA developed a highly integrated ICT system comprising:

- A cognitive software (The VESPA Training Software), developed under several formats (VR 3D, VR 2.5D, etc.), mixing Tasks/Exercises and training specific Cognitive and Executive functions; rehabilitation paths (Protocols) are expressed in terms of training Sessions combining several Tasks in a time slot on a specific device.
- An e-Infrastructure built on top of a cloud computing solution and hosting the necessary services for system operation such as:
  ○ A management Web Application where doctors and caregivers can define treatment paths and monitor the patient's performances (the VESPA Portal);
  ○ A clinical database storing metrics related to the patient's cognitive training activities;
  ○ Other web services necessary to the near real-time management of information produced by the system and the training activities.
- A set of dedicated visualization devices such as:
  ○ A CAVE Virtual Environment, an immersive VR environment where projectors are directed to the 2 to 6 walls of a room-sized cube (source: https://it.wikipedia.org/wiki/Cave_Automatic_Virtual _ Environment);
  ○ Touchable devices such as Tables, TV sets and Tablet PCs;
  ○ Oculus Rift, Quest and Quest2 Head Mounted Display;
  ○ MS Windows 10+ Personal Computers.

The VESPA System combines these elements in order to provide:

- A fully immersive VR 3D cognitive rehabilitation software exploiting the power of CAVE Virtual Environment;
- An Oculus 3D VR rehabilitation App;
- A mobile VR 2.5 App for cognitive rehabilitation for Tablets, Touch-screen tables and TV sets;
- A MS Windows rehabilitation App for Personal Computers;
- A multi-user Web Portal for the management of rehabilitation paths (for doctors) and the monitoring of performances (for caregivers and patients as well).

3.1 Rehabilitation task batteries

The composition of VESPA treatment paths concerns the presence of tasks for the rehabilitation of subjects belonging to two large chronological domains, respectively Adults and Minor-aged.

At this point, assuming the integration of the tasks derived from the 1st Generation VESPA with the new generation tasks, it is possible to state that the series of tasks are seven, respectively organized in the domains.

The total amount of tasks included in the batteries exceeds 100 units, corresponding to the sets described below.

As it can be noted with reference to the adult domain, the batteries are AD (Alzheimer's Disease), ADK (Alzheimer's Disease Cubes), COG (Cognition) and NC (Neuro-cognitive).

The AD battery is composed of tasks specifically implemented for subjects suffering from AD and specifically aimed at treating ecological executive functions, based on everyday life activities, together with personal, spatial and temporal orientation.

The ADK battery is composed of tasks specifically dedicated to subjects suffering from AD and based on cognitive and executive functions training through cube manipulation. The tasks account for the growing difficulty and increasing number of cubes, situations, scenarios, disposition instructions and spatial requests.

The COG battery is composed of tasks generally dedicated to treatment, implementation, exercise and training of cognitive functions, in our case declinable to the whole set of adult pathological conditions included in VESPA (AD, PD, MS). The tasks are meant to train functions in the light of different situations, object manipulations and requests strictly based on realistic clinical needs.

NC battery is composed of tasks fully designed for full immersive VR, dedicated to the training of cognitive, motor and environmental/ecological-oriented requests and instructions, for AD, PD, MS realties.

The batteries referred to the developmental age are dedicated to CD and ID realities, composed and calibrated to enable, train and implement linguistic, communicative, cognitive, basic self-management issues. The batteries are ID (Intellectual Disability), LD (Linguistic Disorders) and CD (Communication Disorders).

The ID battery is composed of tasks aimed at implementing, training and supporting people with ID through activities strictly adherent to selfmanagement, communication abilities implementation (verbal/nonverbal, declarative/proto-declarative), cognitive rehabilitation, cognitive-motor training, executive functioning priming.

The LD battery is composed of tasks including activities reflecting communication training needs. Activities are strictly related to linguistic instructions and expected answers, object (linguistic unities) presentation and repetition/composition/aggregation requests.

The CD battery is composed of tasks aiming at improving communication abilities through the introduction, manipulation, repetition, tracking of objects (both meant as real objects e.g. animals, properly definable objects, human figures etc. and linguistic units such as phonemes, morphemes, syllables, word-sentences and so on) useful for communication implementation in subjects suffering from CD.

Conclusions

The final product will represent a huge technological improvement with reference to CANTAB® and similar systems. They cannot be used for the evaluation and rehabilitation of motor-cognitive functions involving object manipulation by integrating tactile information and trajectory control in 3D movements. In comparison with other ongoing research projects, VESPA is innovative due to the dynamic evolution of software models for the evaluation and cognitive rehabilitation and for the integration of external diagnostic services, such as EEG from DECIDE.

In comparison with other commercial initiatives (see: http://www.mediahospital.com), VESPA offers:

- Fully Immersive experience in a comfortable environment (Virtual Room).
- Patient's finger and gesture tracking, not available on other systems.
- Integration in a unique device of services usually spread over a number of devices.
- Full digitalization of external tools to be used (e.g. tests, puzzles, toys, etc.).
- Tele-supervision through video-conferencing.
- Huge computing and storage capabilities through the integrated and scalable Cloud services.
- Multi-user portal.

The project leads to an extremely dynamic product. The system is flexible and scalable, porting to mobile (on tablet and mobile Virtual Room) and home (on TV sets) formats for domestic use for the evaluation/monitoring and rehabilitation capabilities under study. The system can easily move to new pathologies and promote a different use.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

The authors' contribution

EMM and SMP made a significant contribution to design the research study, draft the manuscript, revise it critically, carry out a comprehensive review of the literature and provide data interpretation. LAMM supported EMM and SMP with drafting and revising the manuscript. All the authors listed had a direct contribution to the work and approved it for publication.

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