Telerehabilitation of cognitive, motor and sleep disorders in neurological pathologies: the REHOME project

(Article begins on next page)

Telerehabilitation of cognitive, motor and sleep disorders in neurological pathologies: the REHOME project

Claudia Ferraris, Giuseppe Pettiti, Gianluca Amprimo
Institute of Electronics, Information Engineering and Telecommunications
National Research Council
Turin, Italy
{claudia.ferraris, giuseppe.pettiti,gianluca.amprimo}@ieiit.cnr.it

Guido Coppo, Danilo Soprani
Synarea Consultants s.r.l.
Turin, Italy
{guido.coppo, danilo.soprani}@synarea.com

Debora Desideri, Roberto Pratola
Research & Innovation Dep
Engineering Ingegneria Informatica SpA
Rome, Italy
{debora.desideri, roberto.pratola}@eng.it

Jacopo Barbagallo, Santina Antinoro
Integrated Solutions srl
Turin, Italy
{jacopo.barbagallo, santina.antinoro}@integratedsolutions.it

Katiuscia Sacco, Irene Ronga
Department of Phsychology
University of Turin
Turin, Italy
{katiuscia.sacco,irene.ronga}@unito.it

Paolo Ariano, Luigi Privitera
Center for Sustainable Future Technologies
Istituto Italiano di Tecnologia
Turin, Italy
{paolo.ariano,luigi.privitera}@iit.it

***Abstract*—Telemedicine and e-health services are considered fundamental pillars to ensure the sustainability of the health system in the next future. In fact, the aging of the population, and the consequent growing percentage of people suffering from neurological pathologies and related disabilities, require more and more resources from healthcare facilities in terms of monitoring and rehabilitation services. Solutions based on Information and Communication Technologies can support new patient care and disease management strategies, by deploying telemedicine applications and services. In this context, the paper presents the integrated platform implemented in the "REHOME" project, for the remote monitoring and rehabilitation of cognitive, motor, and sleep disorders caused by neurological diseases. The solution integrates sensors and innovative methodologies to face patients' and clinical needs by ensuring the continuity of care and rehabilitation services from health facilities to domestic scenarios.**

Keywords—telemedicine, telerehabilitation, remote monitoring, health care platform, motor and cognitive rehabilitation, neurological diseases

I. Introduction

Post-stroke and degenerative neurological conditions are becoming very common in all western countries and especially in Italy, with an ageing population ([1]-[3]). Neurological conditions, such as dementia and Parkinson Disease dramatically impact on patients' quality of life, inducing serious and sometimes permanent disability, often related to motor and cognitive impairments (data from Istituto Superiore di Sanità – Italy). It has been demonstrated that better rehabilitation outcomes are observed when the patients may continue the rehabilitation process at home [4].

ICT solutions can support new patient-care and disease management strategies based on telemedicine and related applications [5], thus moving monitoring and rehabilitation services from healthcare facilities to domestic scenarios [6][7] and favouring the continuous and remote follow-up of patients. However, at-home rehabilitative protocols are not always effective, especially due to the lack of patients' motivation and comfort in the use of digital instruments [4].

In this context, the paper introduces the technological solution implemented in the "REHOME" project [8] which involves 12 partners including 7 industries, 3 research institutions and 2 hospitals. The project focuses on the remote monitoring and rehabilitation of cognitive, motor, and sleep disorders originated by neurological diseases and injuries (such as stroke, Mild Cognitive Impairment and Parkinson's disease), using innovative technologies and methodologies to ensure the continuity of care and rehabilitation. The platform exploits several types of sensors, exergaming and gamification approaches to propose rehabilitation and evaluation exercises suitable for home settings, at the same time facilitating the communication and interaction between doctor, patient, and caregiver. The project was carried out in a multidisciplinary context, integrating the technological competences and the clinical skills of the REHOME consortium to achieve a helpful, complete and integrated solution.

The following sections describe the overall architecture and the individual components of the implemented solution, focusing on objectives, targets, technological devices, and methodologies. The last section contains the concluding remarks, next steps, and innovative features of the REHOME project.

II. The architecture of the solution

The solution implemented in the REHOME project is designed to support the following scenario: a health care professional (HCP), after the initial patient's evaluation, establishes the appropriate rehabilitation plan and delivers a device kit to the patient to start the telerehabilitation. The patient is engaged through the available e-learning and communication functions with the HCP. Afterwards, while the patient performs the assigned exercises, the REHOME system enables telemonitoring capabilities by collecting data related to rehabilitation and health evaluation sessions, thus allowing remote and timely analysis from HCP. In case, the patient incurs in problems or deviates from the planned program, REHOME proactively notifies the HCP.

In last years, home-based rehabilitation has been widely considered by researchers. Many software systems have been developed for this purpose [9], but several challenges are still open [10]. The REHOME system wants to address some of them, such as increasing patient engagement, better understanding the functionality required for different diseases (each with its own peculiarity), managing the personalized rehabilitation plan, and evaluating the effectiveness of remote treatment and the usability of the solution.

As depicted in Fig.1, the REHOME system is distributed and composed of several types of subsystems. Some of these (namely Motor, Cognitive, and Sleep Platforms) are located at the patient's home: they differ in the devices/sensors used and in the application functions they offer according to the rehabilitation program assigned to each patient. Another type of subsystem, namely HCP Platform, is located in hospitals and clinics and offers HCPs the functionalities to monitor patients remotely. The last subsystem is the REHOME Microservices Platform (REHOME-MP), deployed on the cloud, which provides the core functionalities to enable the system to work. Such platform consists of several components, designed according to the micro-services principles as to be extensible and support new future needs of telemedicine-related platforms. Micro-services are small self-contained applications that can be developed and deployed individually by dedicated teams. The primary benefits of this approach are an agile development, a shorter release cycles, and faster time to market, so to better support the continuous improvement of the platform. Each component is introduced to meet clinical and technical requirements. In addition, the micro-service architecture makes it possible to achieve full independence of each individual component as the latter are separate and autonomous and can be replaced, developed, and resized individually.

The whole architecture is designed according to the event-driven pattern to decouple supporting micro-services from disease-specific platforms [11]: this approach enhances scalability and integration of additional platforms.

The core element enabling this pattern is the Event Bus, designed to collect and dispatch data according to the HL7 FHIR R4 standard [12]. One of advantages of this standard is the capability to support RESTful communication over HTTP/s protocol and thus more suitable for mobile clients. The interactions with the Event Bus are mediated by the API Gateway who is responsible of dispatching messages towards the various micro-services, enforcing all the security-related policies. The main micro-services of the REHOME-MP are described hereafter.

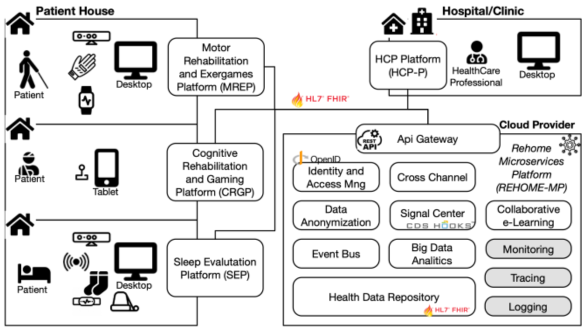

Fig. 1. REHOME system architecture

The Health Data Repository collects, integrates, and shares data coming from the different platforms. The data are harmonized according to the HL7 FHIR data model by leveraging the LOINC common dictionary and managed in compliance with the GDPR requirements as to ensure the safety of the personal data of the patients.

The Big Data Analytics provides services for analysing the heterogeneous amount of data collected. This data span from clinical rehabilitation ones, to continuous monitored ones like bioelectrical signals, up to multimedia contents like video recording of the rehabilitation and sleep sessions. The system deals with managing both real-time analyses (data are processed as soon as they are available) and batch analyses (blocks of data are processed at specific time intervals).

The Signal Center purpose is to notify end-users, about events of interest prior to a subscription procedure. Examples of supported notifications are: "the patient skipped one or more training sessions"; "the score of some exercise is too low"; "time to perform a training session too long", and so on. The system is based on the HL7 CDS-Hooks specification and its cards mechanism [13]. The rules for the generation of the cards are written using HL7 CQL language, specialized for the clinical domain [14]. The data sources for the CQL rules are the Health Data Repository and the new knowledge generated by the Big Data Analysis.

The Cross channel allows to access patient data using voice interaction [15][16]. The project investigated the possibility of translating user intent in FHIR based queries using alternative devices, such as Google home and Amazon Alexa. However, in this context, there are several privacy and compliance issues with the GDPR that needs further investigations and developments.

The Data anonymization produces anonymized datasets starting from data of any FHIR Repository (such as Health Data Repository). The service is configurable and extendable with different anonymization algorithms. The component was created following an Extract, Transform and Load (ETL) process which involves: (1) the extraction of FHIR resources from the Health Data Repository, (2) filtering of relevant attributes, (3) anonymization of the extracted resources [17][18]. Those operations allow the HCPs to select the anonymization properties to apply on specific attributes and, eventually, export data in databases or CSV files.

The Collaborative eLearning enables to support patients during the rehabilitation process through specific functionalities: messaging, calendar, diary, articles, and e-learning courses. It comes with a dedicated mobile application and web widgets (integrated into REHOME-MP). The only two actors involved are the HCP and the patient (or caregiver) to offer high privacy guarantees.

Finally, REHOME-MP introduces some infrastructural services for monitoring purposes, necessary to the distributed nature of micro-services architecture, such as to track in-services remote invocations, centralize service logs and monitor the overall performance of the solution.

III. Cognitive Rehabilitation and Gaming Platform

The Cognitive Rehabilitation and Gaming Platform (CRGP) focuses on training and rehabilitation of specific cognitive functions/domains that are typically compromised in older people with Mild Cognitive Impairment (MCI), which a neurological condition, often prodromal to dementia or Alzheimer. CRGP, however, represents a flexible tool for neuro-cognitive rehabilitation, which can be easily adapted to contrast the cognitive alterations in Parkinson Disease and in post-stroke subjects. CRGP activates cognitive rehabilitation exercises according to the personalized therapeutic plan, thus allowing HCPs to follow patients remotely. The platform includes game-exercises dedicated to train several cognitive domains (such as, attention, memory, and executive functions) to cover as much as possible the clinical-rehabilitation needs of the different patients affected by cognitive impairments.

A. *Single-Domain and Ecological Exercises*

This component delivers to the patient a suite of exercises for cognitive rehabilitation usable through a mobile application for tablets. It consists of three main elements: *scheduler*, the core of the application that receives from REHOME-MP the personalized rehabilitation plan defined by HCPs and proposes the assigned exercises accordingly; *calendar,* which shows the sessions to be performed, and the compliance with the rehabilitation plan; *gamification,* which shows the goals achieved by the patient in a badge form.

The single-domain exercises allow the training of specific cognitive functions, including selective and divided attention; reasoning and planning (executive functions); long-term memory and learning. The implemented exercises use the logic of repetition and gradualness, thus modulating the level of difficulty according to the patient's improvements and current abilities [19]. Furthermore, the exercises are customized using facilitations (cues), feedback and solicitation of new ways to complete the tasks. Patient's involvement and motivation ([20]) are ensured by a gamified approach and through immersive navigation with 360° videos, used to explore the surrounding space and find the hotspots where exercises are activated. Exercises are contextualized to typical contexts of daily life, in order to train cognitive skills for real life.

The ecological exercises are designed for recreating situations similar to reality and daily life [21], allowing to train several cognitive functions at the same time (as it would be in real life). The suite includes two macro-exercises of medium-high difficulty, consisting of single tasks which, linked together, develop a story of about 15 minutes inserted in a playful context. The individual tasks are proposed in different versions, thus ensuring greater variability and allowing the patient to perform cognitive tasks several times to increase the level of learning and improvement.

Gamification techniques are used to improve the involvement and motivation, using typical video-gaming elements to encourage constant exercise and commitment in the long term, to immediately reward and gratify the user for completing the exercise, to cumulate scores, and therefore gratification, during the rehabilitation path.

The exercise results are sent to REHOME-MP for the analytics and remote monitoring by HCPs.

B. *Spatial Memory Domain*

For this cognitive domain, an innovative methodology based on virtual reality has been adopted for immersing patients in highly realistic simulation with multiple stimuli. This aims to control cognitive and emotional aspects as experienced by the user, providing an intense sensation of "presence" in the virtual environment, thus facilitating the transfer of skills acquired or rehabilitated into the real environment [22].

To this end, an interactive 3D game was developed to immerse the patient in an imaginary virtual city and stimulate spatial orientation by exploring the environment and carrying out simple tasks. The 3D game is delivered on both PC and mobile devices (tablets), to be used in domestic contexts. The virtual city is organized into five districts with progressively increasing size, where the garden in the centre represents the starting point. The training goal is to find five components of a bicycle dislocated in the districts: buildings and streets in the city are very similar and few reference points are available to make orientation more difficult and stimulate the creation of cognitive maps using allocentric-mapping strategies [23][24].

Users' interaction is allowed through a mouse and keyboard, virtual keys on the tablet, or a joystick. Results of users' virtual space exploration, as well as users' abilities to retrieve the bicycle components, are recorded and processed to generate game scores to improve players' gratification. Furthermore, exploration results are also sent to the REHOME-MP and shared with HCPs for the remote patient's monitoring.

C. *Cognitive-Motor Rehabilitation Domain*

This domain addresses the evaluation and enhancement of cognitive-motor skills through cognitive exercises for the training and improvement of specific functions, crucial for daily life activities, such as, motor control, motor inhibition, planning of motor responses and attention.

Specifically, a set of exercises in a game environment has been designed according to specific criteria that include: the Weigl's Sorting Test, whose purpose is to measure the ability to grasp superordinate similarities (Categorical Thinking) between different stimuli [25]; collecting specific objects along a path, to evaluate the user's planning ability; count elements displayed and, subsequently, detect them in a list of options; a "go-nogo" task ([26][27]), specifically designed to evaluate motor inhibition skills, where the user has to repeatedly perform a an action (e.g., make avatar jumps) and suddenly stops, when a specific cue is displayed.

The game is based on exploring a virtual 3D desert island, organized in several areas (beach, forest, waterfall, hill) where the exercises are available. The patient explores the island through an avatar that interacts with 2D objects. The graphical user interface (GUI) includes elements about: health status, level progression, score (that progressively increases with exercises execution), character's face with facial expressions consistent with health status.

IV. MOTOR REHABILITATION AND EXERGAMES PLATFORM

The Motor Rehabilitation and Exergames Platform (MREP) focuses on the assessment and rehabilitation of motor impairments typical of Parkinson's disease and post-stroke, but it is also suitable for older people with MCI. MREP activates rehabilitation exercises according to the personalized therapeutic plan and automatically assesses the patient's condition through motor tasks referable to traditional clinical evaluation scales and tests, thus allowing clinicians to follow the patient's improvement or worsening remotely and promptly intervene. MREP includes three components, which employ different sensors and methodologies to cover as much as possible of the clinical and rehabilitation needs of these patients.

A. Assessment of motor condition with RGB-Depth sensors

The component that deals with the assessment of the motor condition is a motion capture system designed to be non-invasive and easy to use, even in an unsupervised scenario. It is based on a single RGB-Depth camera (Microsoft® Azure Kinect DK) that allows the 3D reconstruction of human body movements [28]. In recent years, RGB-Depth sensors have been widely and successfully used in movement analysis of healthy and pathological subjects, for assessment and rehabilitation purposes [29][30]. A processing unit (mini-PC or laptop) and a monitor to provide feedback to the user complete the subsystem, which is configurable according to the patient's condition (customization).

The software for the motion capture mainly relies on the body tracking algorithms of Azure Kinect and hand tracking algorithms of Google® MediaPipe Hand, which respectively provide the 3D skeletal model of body and hand used to analyze and characterize the movements. Custom-written MATLAB® scripts perform the movement analysis by estimating objective and clinically significant kinematic parameters and assigning a summary score to the motor condition through Machine Learning techniques.

The GUI is developed in Unity [31]: the human-machine interaction (HMI) occurs with arm movements on interactive objects displayed on the screen. GUI manages many operations automatically and guides the user in all phases: authentication and download of the personalized rehabilitation plan from REHOME-MP, execution and analysis of motor tasks, data transmission to REHOME-MP. The motor tasks delivered by the subsystem concern upper and lower limbs; posture, balance, and instability; gait; hand dexterity. The tasks are assigned by HCPs to assess the motor condition jointly to rehabilitation exercises.

B. Rehabilitation with exergames in virtual environment

This component offers 3D exergames for motor rehabilitation, immerse in virtual environments and designed according to clinical/therapeutic specifications [32]. The exergames are developed in Unity, adopting a low poly graphics mode, and use the same previously mentioned RGB-Depth sensor to capture and display body movements in virtual scenes.

The goal of the exergames is to allow patients to perform specific motor and cognitive tasks through the game experience that increases their involvement and provides positive feedback that encourages them to continue the rehabilitation/training motor path as planned by HCPs ([33][34][35]). The interaction with the virtual environment occurs through body tracking algorithms, with specific movements required for each exergame. Increasing difficulty levels are also provided to respond adequately to the patient's level of motor disability and improvements, thus stimulating the patient to pursue new goals and game results. The exergames are activated according to the personalized rehabilitation plan. Game and kinematic parameters are sent to the REHOME-MP through the motor assessment subsystem.

Three exergames have been developed based on consolidated rehabilitation techniques, recreating a 3D virtual game environment where the patient's movements are "captured and synchronized" in real-time: Cross-country skiing, Airplane, and Keyboard. Each exergame involves a precise method of execution that includes repetitive, alternating and pointing movements of the upper limbs and trunk flexion movements (particularly challenging for pathological subjects) while the patient is seated in front of the RGB-Depth sensor.

Particular attention was paid to the design of a "user-friendly" HMI; the configurability of difficulty levels to intercept the specific patient's disabilities (personalization); aspects of gamification to stimulate the patient to achieve ever-greater goals.

C. Upper limb Rehabilitation with EMG

This component deals explicitly with the upper limb motor assessment using surface electromyography (sEMG) for rehabilitation purposes ([36][37]). It is based on REMO® (Morecognition Srl, Turin, Italy), a wearable armband composed by 8 bipolar dry electrodes for detecting muscles activation of the forearm and classifying movements performed. The device works in real-time and, through the Latent Dirichlet Allocation (LDA) algorithm, can recognize if movements performed are the same recorded in the calibration phase [38]. A standalone application completes the solution: it is used for device management and to provide visual feedback to the patient according to the amplitude of the detected sEMG signal.

Some typical movements, used to assess the hand motor dysfunctions in clinical practice (such as finger extension, cylindrical grasp, and spherical grasp), have been included to monitor the muscle activation of patients. The system counts and evaluates the number of complete hand movements performed in a maximum time and provides visual feedback on the GUI based on the sEMG signals and the correctness of movement execution.

The application connects to the REHOME-MP for authentication and downloading the personalized rehabilitation plan. At the end of each session, the outcomes related to muscles activation during the assessment phases are sent to REHOME-MP for remote monitoring by HCPs.

V. Sleep Evaluation Platform

The sleep evaluation platform (SEP) component aims to detect and evaluate sleep disorders, focusing on PD and post-stroke subjects [39]. The evaluation consists in identifying different sleep stages through visual scoring of the polysomnography (PSG). PSG includes many signals such as electroencephalogram (EEG), electromyography (EMG), electrocardiogram (ECG), electrooculogram (EOG), pulse oximetry, respiration and Periodic Leg Movements occurring during Sleep (PLMS). The PSG makes it possible to observe sleep efficiency, sleep quality, and sleep.

To this end, the system uses a combination of non-invasive wireless sensors to assess and report sleep patterns. For standard PSG acquisition, a group of sensors has been adopted, including some off-the-shelf equipment and a set of prototypal wearable sensors (chest strap, cap, and socks) specifically developed in sensorized fabric (ASTEL Srl, Pavone Canavese, Turin, Italy). An environment sensor has been added to measure room noise, temperature, humidity, and illumination. The commercial pressure band Emfit QS (Emfit Ltd, Vaajakoski, Finland) supplies information on the presence in bed, the quantity of movement, and measures of heart rate and breath rate. Finally, an RGB-Depth camera, which mounts an infrared camera, has been added to provide video documentation of relevant events occurring during the night and infer more accurate information on specific limb movements [40].

Sleep monitoring sessions are scheduled based on a personalized therapeutic plan: the modular architecture permits activating only the sensors necessary for specific monitoring, thus minimizing patient discomfort during the night. SEP is designed to ensure high usability and flexibility in clinical and domestic settings. In both cases, a very simple web interface allows the user (specialist in clinical settings or patient in domestic settings) to manage the system with smartphones or PCs. A mini-PC completes the system: it deals of sensors functioning and management, data storing, signal processing and the transfer of processed data to the REHOME-MP.

At the end of each sleep session, the system analyses the acquired data to perform automatic sleep staging [41][42], thus producing an hypnogram of the different sleep phases (REM, N-REM levels, awakening), and assigning a score to the sleep quality. All substantial data and video clips of relevant events detected during sleep are sent to the REHOME-MP for further examination and analysis.

VI. HCP Platform

The HCP Platform allows management of patient data and personalized rehabilitation plans for the supported diseases (e.g., scheduling of evaluation sessions or exercises with personalised settings). It also provides support for visualizing monitored data and notification mechanisms for evaluating the rehabilitation's sessions through: a) generic dashboards (common to the various diseases) summarizing the salient data in graphs and diagrams (like scores, times, adherence, statistics, variations over time of variables of interest); (b) specific dashboards for each disease tailored according needs and requirements of each platforms (like views for specific data or domain specifics graphs).

VII. Conclusion

The REHOME system aims to overcome some weaknesses of telerehabilitation, such as lack of patient's motivation and comfort in use of digital tools. This happened thanks to a close collaboration between HCPs and technicians in order to collect the patients' needs and address them through the system requirements.

Furthermore, we adopted a systematic gamified approach matched with the selection of aesthetically pleasing backgrounds, which has been demonstrated to support patients' motivation and learning outcomes ([22][43][44]).

In the end, with the aim of improving patients' compliance with the digital tools included in the rehabilitation program, the project focused on usability tests. Clinicians, researchers, and technicians selected the best solutions to maximize patients' compliance and technical reliability.

Part of the innovation of REHOME project is related to a novel integrated approach to evaluate its effectiveness. Several different assessments techniques were matched, with the aim of maximizing the chance to faithfully track the modulation of patients' performances. Besides neuropsychological tests and online behavioural evaluation of patients' performances, specific in-presence electrophysiological protocols were realized to monitor patients' rehabilitation pattern ([45][46][47]). The experimental phase of REHOME is currently underway and will involve more than 80 patients. Preliminary results on usability and the platform's ability to train and characterize the different functional aspects are promising. However, it is necessary to wait until the end of the project to evaluate the effectiveness of the specific treatments provided through the REHOME system.

Overall, the REHOME system has the potential to provide different insights and clinical advantages. From a research perspective, the integrated assessment approach adopted for the REHOME project may provide further insights for identifying the most sensitive markers to track patients' performances and changes in health conditions. From a technological and clinical perspective, the REHOME system is modular, extensible, and customizable to be easily adapted to the future and specific needs of patients and HCPs.

Recently, several review studies ([5][6][7][9]) have analyzed ICT solutions in the literature, highlighting strengths and limitations. Compared to the state-of-the-art, the REHOME system differs in some innovative aspects, including: (a) development and integration of sensors and algorithms to collect different types of data and bio-signals for a more comprehensive analysis of patients' general condition and treatment effects; (b) gamification and virtual exergames to cover different domains to be evaluated and trained, with particular attention to patients' engagement, needs, and aesthetic preferences [44]; (c) personalization of treatment as type and difficulty of exercises can be fully customized according to patients' needs and progress in the therapeutic plan to stimulate new rehabilitation goals; (d) usability and easy interaction thanks to specially designed GUIs to facilitate the use of individual platforms even in unsupervised and domestic scenarios.

In conclusion, REHOME system may be considered a proper e-health tool that addresses the need for technological innovative and highly flexible rehabilitation tools, thus satisfying the guidelines of Horizon Europe and Italian PNRR (https://italiadomani.gov.it/it/home.html).

Acknowledgment

The REHOME project was funded by Piemonte Region's, 2014-2020 Regional Operational Programme (ROP) under the European Regional Development Fund (ERDF). We also thank M.D. Vittoria Tibaldi (Unit of Geriatrics, Molinette Hospital, City of Health and Science of Turin, Turin, Italy), Giorgia Pregnolato (Laboratory of Rehabilitation Technologies, IRCCS San Camillo Hospital, Venice, Italy) and Margherita Urso (ASTEL Srl) for their contribution in the finalization of this work.

References

[1] World Health Organization, "World Report on Ageing and Health,", 2015, ISBN 978-92-4-156504-2

[2] United Nations Department of Economic and Social Affairs, Population Division, "World Population Ageing 2020 – Highlights", 2020, ISBN: 978-92-1-148347-5 (SR/ESA/SER.A./451)

[3] Y. Béjot and K. Yaffe, “Ageing Population: A Neurological Challenge,”, Neuroepidemiology, vol. 52, pp.76-77, February 2019.

[4] B. Steiner, B. Saalfeld, et al. “OnTARi: an ontology for factors influencing therapy adherence to rehabilitation”. BMC Medical Informatics and Decision Making, vol. 21(1), pp. 1-14, May 2021

[5] S.A. Tabish and S. Nabil, “Future of Healthcare Delivery: Strategies that will Reshape the Healthcare Industry Landscape,”, Int. J. Sci. Res., vol. 4(2), pp.727-758, February 2015.

[6] N. Fares, R.S. Sherrattand I.H. Elhajj, “Directing and Orienting ICT Healthcare Solutions to Address the Needs of the Aging Population,”, Healthcare (Basel),vol. 9(2), 147, February 2021.

[7] A. Gallucci, et al., “ICT technologies as new promising tools for the managing of frailty: a systematic review,”, Aging Clin Exp Res., vol. 33(6), pp. 1453-1464, July 2020.

[8] REHOME Site, https://progetto-rehome.it/ (Last Access: March 2022)

[9] M. Hosseiniravandi, A.H. Kahlaee, H. Karim, L. Ghamkhar, R. Safdar, “Home-based telerehabilitation software systems for remote supervising: a systematic review,”. IntJ Technol Asses Health Care ournal of technology assessment in health care, vol. 36(2), pp. 113–125, March 2020.

[10] N. Rabanifar, K. Abdi, “Barriers and Challenges of Implementing Telerehabilitation: A Systematic Review”, Iranian Rehabilitation Journal, vol. 19 (2), pp. 121-128, 2021

[11] R. Laigner, et al., “From a monolithic big data system to a microservices event-driven architecture,”, 46th Euromicro Conference on Software Engineering and Advanced Applications (SEAA), IEEE, August 2020.

[12] FHIR HL7 R4, https://www.hl7.org/fhir/ (Last Access: March 2022)

[13] FHIR CDS-HOOKS, https://cds-hooks.hl7.org/ (Last Access: March 2022)

[14] FHIR CQL, https://cql.hl7.org/ (Last Access: March 2022)

[15] S. Tian, W. Yang, J.M. Le Grange, P. Wang, W. Huang, Z. Ye, “Smart healthcare: making medical care more intelligent,” Global Health J., vol. 3, pp. 62-65, September 2019.

[16] E. Sezgin, Y. Huang, U. Ramtekkar, et al, “Readiness for voice assistants to support healthcare delivery during a health crisis and pandemic”. Npj Digit. Med., vol. 3, 122, September 2020.

[17] F. Kohlmayer, F. Prasser, C. Eckert, K. A. Kuhn, “A flexible approach to distributed data anonimization”. J Biomed Infor, vol. 50, pp. 62-76, August 2014.

[18] P. Grace (ITI), A. Zigomitros (UPRC), A. Papageorgiou (UPRC), C. Patsakis (UPRC), F. Casino (External, UPRC), M. Pocs (STL). “Guidelines for data anonymization report”. OPERANDO (2016). (Available online: http://www.operando.eu/upload/operando/moduli/D4.3Guidelinesfordataanonymizationreportv1.0_77_326.pdf, Last Access: March 2022)

[19] L. Clare and B. Woods, “Cognitive rehabilitation and cognitive training for early-stageAlzheimer’s disease and vascular dementia,”, Cochrane Database Syst Rev, vol. 4, CD003260, 2003.

[20] P. Iannizzi, et al. “Il training cognitivo per le demenze e le cerebrolesioni acquisite,”, pp. 1-198, 2015, ISBN: 9788860307538

[21] P.W. Burgess, et al. “The case for the development and use of "ecologically valid" measures of executive function in experimental and clinical neuropsychology,”,. Int Neuropsychol Soc., vol. 12(2), pp. 194-209, March 2006.

[22] K. Sacco, I. Ronga, P. Perna, et al.,. “A virtual navigation training promotes the remapping of space in allocentric coordinates: evidence from behavioral and neuroimaging data”. Frontiers in Human Neuroscience. 10.3389/fnhum.2022.693968. (in press)

[23] L. Carelli, M.L. Rusconi, et al. “The transfer from survey (map-like) to route representations into Virtual Reality Mazes: effect of age and cerebral lesion”. J NeuroEngineering Rehabil, vol. 8, 6, January 2011.

[24] L. Latini-Corazzini, M.P. Nesa, et al. “Route and survey processing of topographical memory during navigation”. Psychological Research, vol. 74(6), pp: 545–559, February 2010.

[25] M. Laiacona, M.G. Inzaghi, et al. “Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test”, Neurol Sci., vol. 21(5), pp.279-91, October 2000.

[26] M. Angelini, et al. “Motor inhibition during overt and covert actions: An electrical neuroimaging study”. PLoS One, vol. 10, e0126800, May 2015.

[27] A.T. Nguyen, J.J. Moyle and A.M. Fox “N2 and P3 modulation during partial inhibition in a modified go/nogo task”. Int. J. Psychophysiol. Vol. 107, pp. 63–71, September 2016.

[28] J.A. Albert, et al., “Evaluation of the Pose Tracking Performance of the Azure Kinect and Kinect v2 for Gait Analysis in Comparison with a Gold Standard: A Pilot Study,”, Sensors (Basel), vol. 20(18), 5104, September 2020.

[29] R.A. Clark, et al. “Three-dimensional cameras and skeleton pose tracking for physical function assessment: A review of uses, validity, current developments and Kinect alternatives,”. Gait & Posture, vol. 68, pp.193-200, February 2019.

[30] A. Askin, et al., “Effects of Kinect-based virtual reality game training on upper extremity motor recovery in chronic stroke,”, Somatosensory & Motor Research, vol. 35(1), pp. 25-32, March 2018.

[31] UNITY Real-Time Development Platform, https://Unity.com (Last Access: March 2022)

[32] A. Garcia-Agundez, et al., “Recent advances in rehabilitation for Parkinson's Disease with Exergames: A Systematic Review,”, J Neuroeng Rehabil, vol. 16(1), 17, January 2019.

[33] G. Barry, et al. “The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence,”, J Neuroeng Rehabil., vol. 11, 33, March 2014.

[34] I. Chiuchisan, et al., “Future Trends in Exergaming using MS Kinect for Medical Rehabilitation,”, Int. Conference and Exposition on Electrical And Power Engineering (EPE), pp. 0683-0687, October 2018.

[35] H.C. Lee, et al., “The Effect of a Virtual Reality Game Intervention on Balance for Patients with Stroke: A Randomized Controlled Trial,”, Games Health J., vol. 6 (5), pp. 303-311, October 2017.

[36] I. Mileti, et al. “Muscle Synergies in Parkinson's Disease,”, Sensors (Basel). vol. 20 (11),3209, June 2015.

[37] J.E. Thorp, et al., “Monitoring Motor Symptoms During Activities of Daily Living in Individuals With Parkinson’s Disease,”, Front. Neurol. vol. 9, 1036, December 2018.

[38] N. Celadon, S. Došen, I. Binder et al. “Proportional estimation of finger movements from high-density surface electromyography”, J NeuroEngineering Rehabil vol. 13, 73, August 2016.

[39] S. Fallmann and L. Chen, “Detecting chronic diseases from sleep-wake behaviour and clinical features”, in Proc. IEEE 5th Int. Conf. Syst. Inform., pp. 1076-1084, November 2018.

[40] J. Lee, M. Hong and S. Ryu, “Sleep monitoring system using kinect sensor”, Int. J. Distrib. Sensor Netw., vol. 11(10), 875371, October 2015.

[41] Mendonça, Fábio, et al. “A review of approaches for sleep quality analysis”, Ieee Access, vol. 7, pp. 24527-24546, February 2019.

[42] O. Faust, et al. “A review of automated sleep stage scoring based on physiological signals for the new millennia”, Comput Methods Programs Biomed, vol. 176, pp: 81-91, July 2019.

[43] M. de Castro-Cros, M. Sebastian-Romagosa, et al. “Effects of gamification in BCI functional rehabilitation”, Front Neurosci, vol. 14, 882, August 2020.

[44] P. Sarasso, M. Neppi-Modona, K. Sacco and I. Ronga “‘Stopping for knowledge’: The sense of beauty in the perception-action cycle”. Neurosci Biobehav Rev, vol .118, pp. 723-738, November 2020.

[45] P. Sarasso, M. Neppi-Modona M, et al. “Nice and Easy: Mismatch Negativity Responses Reveal a Significant Correlation Between Aesthetic Appreciation and Perceptual Learning”. J Exp Psychol Gen, November 2021 (in press).

[46] P. Sarasso, I. Ronga, M. Neppi-Modona and K.Sacco “The Role of Musical Aesthetic Emotions in Social Adaptation to the Covid-19 Pandemic”, Front Psychol, vol. 12, 611639, March 2021.

[47] P. Sarasso, P. Perna, et al. “Memorisation and implicit perceptual learning are enhanced for preferred musical intervals and chords”. Psychon Bul Rev, vol. 28 (5), pp. 1623-1637, October 2021.