



IL RETTORE

Vista la Legge 9 maggio 1989, n. 168 - Istituzione del Ministero dell'Università e della ricerca scientifica e tecnologica e ss.mm.ii;

Visto lo Statuto dell'Università degli Studi di Genova;

Visto il Regolamento Generale di Ateneo;

Visto il Regolamento di Ateneo per l'Amministrazione, la Finanza e la Contabilità;

VISTA la legge 7 agosto 1990, n. 241 recante "Nuove norme in materia di procedimento amministrativo e di diritto di accesso ai documenti amministrativi" pubblicata sulla Gazzetta Ufficiale n. 192 del 18/08/1990 e s.m.i.;

VISTO il Decreto del Presidente della Repubblica 28 dicembre 2000, n. 445 (Disposizioni legislative in materia di documentazione amministrativa) e s.m.i.;

VISTO il Decreto Direttoriale MUR n. 341 del 15/03/2022 di emanazione di un Avviso pubblico per la presentazione di Proposte di intervento per la creazione di "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" nell'ambito del Piano Nazionale di Ripresa e Resilienza, Missione 4 "Istruzione e ricerca" – Componente 2 "Dalla ricerca all'impresa" – Investimento 1.3, finanziato dall'Unione europea – NextGenerationEU";

VISTO il Decreto Direttoriale MUR n. 1553 dell'11/10/2022 di concessione del finanziamento del progetto Codice identificativo PE00000006, Acronimo MNESYS, Titolo "*A multiscale integrated approach to the study of the nervous system in health and disease*", registrato alla Corte dei conti il 23/11/2022 al n. 2948 e relativi allegati;

CONSIDERATO che l'Università degli Studi di Genova è leader dello Spoke 6, dal titolo "*Neurodegeneration, trauma and stroke*";

CONSIDERATO che gli Spoke possono emanare – nell'ambito dei limiti e con le modalità previste dall'Avviso – "bandi a cascata" finalizzati alla concessione di finanziamenti a soggetti esterni per attività coerenti con il progetto approvato;

VISTO il Decreto del Direttore Generale n. 5418 del 14 novembre 2023 di nomina del Responsabile del Procedimento;

VISTA la delibera della seduta del 28 marzo 2024 con cui il Consiglio di Amministrazione dell'Università degli Studi di Genova ha approvato il modello del "Bando a Cascata" per Micro, Piccole, Medie e Grandi Imprese che il presente Avviso ha adottato;

VISTO il Decreto del Rettore n. 2982 del 11 giugno 2024 di emanazione del Bando a cascata per il finanziamento di proposte di intervento per le attività di ricerca svolte da Micro, Piccole, Medie e Grandi Imprese nell'ambito del programma di ricerca MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*", per lo Spoke 6 dal titolo "*Neurodegeneration, trauma and stroke*", nell'ambito del PNRR, Missione 4, Componente 2, Investimento 1.3 – finanziato dall'Unione europea – NextGenerationEU (CUP D33C22001340002);

VISTI i riferimenti normativi comunitari, nazionali citati nella suddetta delibera e nel Bando a cascata, che si intendono integralmente richiamati e parte sostanziale del presente documento;

CONSIDERATO che alla data di scadenza per la presentazione delle proposte progettuali, fissata entro e non oltre il giorno 1 luglio 2024, per la Tematica D – “Development of an interactive and adaptive telemedicine cognitive rehabilitation module for the prevention of cognitive decline in the elderly” era pervenuta a mezzo PEC all’indirizzo air3@pec.unige.it la seguente proposta:

- **PROPONENTE:** KHYMEIA Srl
- **TITOLO PROPOSTA:** Cogniweb - A WEB-based interactive and adaptive telemedicine COGNitive rehabilitation module for the prevention of cognitive decline in the elderly;

TENUTO CONTO che la Responsabile del procedimento, Ing. Patrizia Cepollina, ha ritenuto ricevibile, ammissibile e conforme la proposta esaminata la documentazione integrativa con prot. 6279/2024 del 22.10.2024;

CONSIDERATO che nel Bando è previsto che la valutazione di merito tecnico-scientifico dei progetti pervenuti sia affidata ad una Commissione composta da almeno tre esperti esterni al Partenariato, indipendenti e competenti dell’Area tematica dello Spoke;

VISTO il Decreto Rettorale n. 6614 del 20 dicembre 2023 con cui è stato emanato l’Avviso di manifestazione di interesse per la costituzione di un albo di esperti indipendenti a supporto della valutazione di merito dei progetti PNRR presentati sui bandi a cascata del progetto MNESYS – *A multiscale integrated approach to the study of the nervous system in health and disease*;

VISTO il DR 855 del 20/02/2024 con il quale è stato istituito l’Albo a supporto della valutazione scientifica dei progetti presentati in risposta al bando pubblico per la selezione di proposte progettuali da finanziare nell’ambito delle attività di ricerca dello Spoke n. 6 di cui al programma di “MNESYS - *A multiscale integrated approach to the study of the nervous system in health and disease*”;

VISTO il verbale del 30/09/2024 il Comitato Scientifico del programma di ricerca MNESYS, costituito dal Prof. Sergio Martinoia, Prof. Antonio Uccelli e Prof. Tullio Florio, con cui si procede all’utilizzo di tale Albo per l’individuazione di tre valutatori idonei alla creazione di una Commissione per il Bando a cascata per Micro, Piccole, Medie e Grandi Imprese;

VISTO il Decreto Rettorale n. 4721 del 8 ottobre 2024 con cui è stata nominata la commissione di valutazione delle proposte pervenute in risposta al bando a cascata di cui al Decreto del Rettore n. 2982 del 11 giugno 2024, indicato nelle premesse del presente decreto;

ACQUISITO il verbale della Commissione di valutazione della seduta del 11/11/2024 (Prot. n. 113647/2024)

VISTO il Decreto Rettorale n. 5612 del 18.11.2024 con cui è stata approvata la proposta “Cogniweb” presentata da Khymeia srl in risposta al bando a cascata emanato con Decreto Rettorale n. 2982 del 11 giugno 2024, indicato nelle premesse del presente decreto;

TENUTO CONTO che in data 22/11/2024 è stata inviata a Khymeia srl la comunicazione Prot. n. 118438 in cui si rendevano noti gli esiti della procedura e si richiedeva la documentazione propedeutica all’adozione del provvedimento di ammissione del finanziamento;

CONSIDERATO che in data 13/12/2024 (Prot. 128605/2024 del 13/12/2024) è stata richiesta una integrazione per regolarizzare le dichiarazioni propedeutiche necessarie;

TENUTO CONTO che la documentazione a integrazione, ricevuta da Khymeia srl con comunicazione Prot. n. 129739/2024 del 16.12.2024 è stata ritenuta conforme a quanto previsto nel bando a cascata di cui al

Decreto del Rettore n. 2982 del 11 giugno 2024, indicato nelle premesse del presente decreto;

DECRETA

ART. 1

L'ammissione a finanziamento del progetto "Cogniweb - A WEB-based interactive and adaptive telemedicine COGNitive rehabilitation module for the prevention of cognitive decline in the elderly" proposto da Khymeia srl - come rappresentato negli Allegati B e C alla proposta presentata con domanda di partecipazione Prot. n. 61699 del 02.07.2024.

ART. 2

L'entità dell'agevolazione concessa, a fondo perduto, ammonta a 99.954,50 euro complessivi come rappresentati nell'allegato C alla proposta presentata con domanda di partecipazione Prot. n. 61699 del 2/07/2024 di seguito riportati:

Allegato C - Piano economico e finanziario			
Dimensione impresa		%Contributo	
Piccola impresa	Ricerca fondamentale	100%	
Dimensione Impresa	Voce di costo	Ricerca Fondamentale	TOTALE
Piccola impresa	Personale dipendente specificamente destinato a realizzare il progetto secondo i costi standard previsti	60.830,00 €	60.830,00 €
	Costi per materiali, attrezzature e licenze		0,00 €
	Costi per servizi di consulenza specialistica purché essenziali per l'attuazione del progetto	30.000,00 €	30.000,00 €
	Costi indiretti determinati forfaitariamente e pari al 15% dei costi ammissibili per il personale	9.124,50 €	9.124,50 €
	Costi per altre tipologie di spese direttamente imputabili al progetto		0,00 €
	TOTALE	99.954,50 €	99.954,50 €

L'agevolazione è pari al 100% dei costi di progetto trattandosi di attività di ricerca fondamentale. L'agevolazione è concessa a valere sui fondi PNRR assegnati a finanziamento al Programma MNESYS Codice PE00000006 a valere sulla Missione 4, Componente 2, Investimento 1.3 – Creazione di "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" ai sensi del Decreto di concessione n. 1553 del 11 ottobre 2022, registrato alla Corte dei Conti il 23/11/2022 al n. 2948, iscritto al Bilancio di Ateneo sul progetto UGOV 100033-2022-TF-PNRR-PE_MNESYS_BANDI_CASCATA.

Il C.U.P. (Codice Unico di Progetto di investimento pubblico) relativo al progetto agevolato sul presente bando risulta essere il seguente: D33C22001340002. Il suddetto CUP dovrà essere riportato sugli originali di tutti i titoli di spesa ammessi ad agevolazione, nonché sulla relativa documentazione attestante i pagamenti.

Si precisa che ai sensi del punto 9 comma 2 del Decreto 31 maggio 2017 n. 115, è avvenuto l'inserimento delle informazioni relative al presente atto di concessione nel Registro nazionale aiuti ed è avvenuta l'interrogazione dello stesso.

Il Codice Concessione RNA - COR rilasciato all'impresa, relativamente alla quota di contributo a fondo

perduto ad essa assegnata, è il seguente:

Ragione sociale	Partita IVA /Codice Fiscale	COR
KHYMEIA SRL	03345930287	23241819

ART. 3

Le attività, come indicate dettagliatamente nell'Allegato B alla domanda di finanziamento, dovranno essere avviate a partire dalla data di sottoscrizione del Contratto e concluse entro e non oltre 10 mesi affinché siano rendicontate in tempo utile per consentire la chiusura del programma PE MNESYS il cui termine è attualmente previsto al 31 ottobre 2025.

Potrà essere valutata e concessa una sola proroga in presenza di ritardi dovuti a circostanze eccezionali e non dipendenti da scelte del Beneficiario esclusivamente nel caso in cui il MUR, a sua volta, proroghi il termine del Programma MNESYS.

ART. 4

Il presente atto sarà pubblicato sul sito UniGe <https://unige.it/progetti-finanziati-dal-pnrr> e laddove la normativa vigente lo richiede.

Il documento informatico originale sottoscritto con firma digitale sarà conservato presso l'Area Ricerca, Trasferimento Tecnologico e Terza Missione.

Allegati:

Allegato B – Proposta progettuale

Allegato C – Piano economico-finanziario

IL RETTORE
Prof. Federico Delfino
(documento firmato digitalmente)



ANNEX B

PE00000006

**“A multiscale integrated approach to the study
of the nervous system in health and disease”**

MNESYS

SPOKE N. 6

Research proposal

Topic addressed by the project: Development of an interactive and adaptive telemedicine cognitive rehabilitation module for the prevention of cognitive decline in the elderly

Proposal: “**COGNIWEB:** a WEB-based interactive and adaptive telemedicine COGNitive rehabilitation module for the prevention of cognitive decline in the elderly”

- Name of the PIs' host institution for the project: Khymeia S.r.l.
- Name of the Principal Investigators (PIs): Eng. Marco Pirini, Ph.D.
- Proposal duration in months: 12



ROLE IN THE PROJECT	NAME	SURNAME	DEPARTMENT	QUALIFICATION	YOUNG (under 40 al 31.12.2024)	F/M
Principal Investigator	Marco	Pirini	R&D department	Biomedical Engineer, Ph.D. Khymeia's R&D Manager	No	M
co-Principal Investigator (co-PI)	Marialuisa	Bullo	R&D Department	Biomedical Engineer. Khymeia's Responsible for Cognitive packages development	Yes	F
Team Member	Massimiliano	Leoni	R&D Department	Developer and product specialist for Khymeia.	Yes	M

1 ABSTRACT

Dementia, particularly Alzheimer's disease (AD), is a major public health concern, necessitating innovative solutions to support patients and their families. Telehealth offer a promising avenue for continuous care, with telerehabilitation emerging as a key component. This proposal aims to implement a scientifically validated network-based cognitive rehabilitation package into a web-based platform (CogniWeb).

The cognitive training (CT) program, developed by Prof. Annalena Venneri's research group, aims to enhance neurocognitive functioning through exercises that engage multiple cognitive domains. These exercises are designed to stimulate the Default Mode Network (DMN), which is particularly affected in AD. Previous studies have shown that CT can increase functional connectivity in the DMN, leading to cognitive improvements in individuals with mild cognitive impairment (MCI) and early-stage AD.

CogniWeb aims to develop a web-based CT program to prevent cognitive decline in patients with MCI and early AD. The program will include 20+ specific cognitive exercises, organized into protocols for 4-week treatment sessions, ensuring interactivity, adaptability, and ease of use. CogniWeb will enable patients to receive treatment from home, ensuring continuity of care and accessibility for older adults with physical limitations. The implementation will leverage Khymeia's existing Medico Amico platform, integrating audio-visual communication, personalized rehabilitation plans, and real-time monitoring to manage multiple patients effectively.

CogniWeb workplan spans 12 months and includes the design of exercises, content creation, implementation, usability validation, and preparation for clinical trials. CogniWeb aims to provide an effective and economically sustainable telerehabilitation tool to improve cognitive health and functional connectivity in patients with MCI and early AD in the context of large-scale adoption by public health organizations.



2 RESEARCH PROPOSAL

2.1 Section a. State-of-the-art and objectives

Dementia is a debilitating condition and a global public health priority, requiring innovative solutions to support patients and families, particularly those affected by Alzheimer's disease (AD) (WHO, 2017). With rapid advancements in communication technology and the urgent need for continuous care, telehealth initiatives have gained worldwide attention (Brigo, 2022). Telehealth encompasses all healthcare services delivered remotely, with tele-rehabilitation emerging as a promising concept in rehabilitation services. Studies have shown that cognitive rehabilitation and physical activity can preserve cognitive health, maintain brain structure, and reduce dementia risk (Cao, 2023; Mukaetova-Ladinska, 2023). However, despite these benefits and the high prevalence of dementia, there is a scarcity of home-based randomized controlled trials (RCTs) proving the effectiveness of cognitive tele-rehabilitation treatments.

This proposal aims to address this gap by implementing a network-based cognitive rehabilitation package into a virtual platform. This web-based platform will be accessible to both therapists and patients, maximizing usability and availability. It is designed to support large-scale adoption in public health programs, making cognitive rehabilitation more accessible to patients, elderly individuals, and therapists.

Let's examine the content of this proposed telerehabilitation treatment and its rationale.

"Cognitive training" (CT) is a label used to describe paper-and-pen or computerized exercises designed to engage a desired set of mental skills for the purpose of enhancing neurocognitive functioning. Although the literature on the topic is considerably rich (on PubMed, for the sole 2023, the use of "cognitive training" as title keyword returns 123 results), very few studies pose the fundamental question: "How does CT work?", or, more precisely, "Based on which computational mechanisms would engaging in CT result into meaningful changes in outcome measures?"

The research group lead by Prof. Annalena Venneri has developed, tested and validated a software-based cognitive training set of activities aimed at inducing synchronized activity of selected brain regions. Referring to Alzheimer's disease as the primary diagnosis of interest, the underlying principle defining the hypothesis from the group was that repeated task-related co-activation of multiple areas would result in increased resting-state functional connectivity among those areas (Martínez et al., 2013). On the basis that Alzheimer's pathology selectively affects the brain's default-mode network (Seeley et al., 2009; Pasquini et al., 2017), the group designed a set of computerized exercises aimed at inducing co-activation of central hubs of this network. Semantic processing, memory retrieval, logical reasoning, and executive processing were identified as computational domains adequate for the purpose and, at the same time, suitable for implementation into computerized exercises. Visuospatial and verbal materials were used to create computational activities which would rely on multiple cognitive abilities. As the main objective of each task was to tap distant hubs of the DMN concurrently, specific cognitive operations suitable for being combined in one task were selected.

Tasks in the CT program (involved to explicitly multi-tap the DMN) were: tasks based on semantic retrieval, rule the odd one out tasks (with both images and text stimuli) dual category tasks, semantic inhibition tasks, tasks based on logical reasoning, sequence completion tasks (with both images and words, tasks based on response times (with multiple types of stimuli included), and a mind twister filler tasks.

The CT program has been widely tested, investigated and verified in terms of its mechanisms of action, and validated in terms of effectiveness:

- De Marco et al. (2016) tested a CT protocol based on DMN stimulation on healthy adults, finding significant increases in the functional connectivity of the posterior DMN. This study provided the basis

for the application of this protocol on patients with MCI, demonstrating that CT can induce lasting changes in brain connectivity even in healthy individuals, suggesting potential preventive benefits.

- The study by De Marco et al. (2018) applied a CT program on patients with MCI, showing that training increased functional connectivity in the left parietal region of the DMN. Although no significant changes were observed in other connectivity networks, the increase in DMN was positively correlated with cognitive improvements, supporting the idea that CT may lead to clinically relevant benefits in brain function in the early stages of Alzheimer's disease.
- The article by Manca et al. (2021) investigated the effects of cognitive training (CT) on patients with mild cognitive decline (MCI) using a computerized exercise program. The results demonstrated a significant increase in functional connectivity in participants' Default Mode Network (DMN), with improvements observed in semantic fluency tests and cognitive rating scales. This supports the hypothesis that CT may be effective in improving brain connectivity and cognitive performance in patients with MCI.
- The study by Venneri et al. (2021) explored the mechanisms underlying CT for neurodegenerative diseases, focusing on DMN. Using computerized exercises, the researchers observed an increase in functional connectivity in the central regions of the DMN, which was associated with improvements in cognitive testing. This suggests that CT can induce significant changes in neural networks involved in cognition.
- Bentham et al. (2021) examined the effect of cerebrovascular loading on CT response in patients with MCI. The study found that a high white matter hyperintensity burden was associated with fewer changes in DMN connectivity after CT. However, CT has been shown to improve functional connectivity in patients with lower cerebrovascular load, indicating the importance of considering vascular factors in the design of CT interventions.

Generally, exercises and activities were organized in protocols lasting 20 daily sessions on 4 weeks, with 5 or more exercises per session, in order to engage the subject for about an hour per session. The CT programs were not tailored on individual performance but difficulty level changed progressively from session to session, and this was kept constant across all participants. Daily activities were generally selected at random before the beginning of the training. Particular effort was put to set a gradually-increasing difficulty level along the twenty days of training, to ensure that the program was homogeneously challenging for its entire duration, as the participants proceeded throughout the training schedule. Apart from the speed of processing tasks, the stimuli remained on screen until the participants gave their response. Although the training was centered on accuracy, rather than response time, the participants were asked to respond as soon as they had solved a trial.

Aim of the project

To develop a web-based program of cognitive exercises for telerehabilitation, aimed at preventing cognitive decline in patients with mild cognitive impairment (MCI) and in the early stages of Alzheimer's disease, based on the aforementioned CT programs.

2.2 Section b. Methodology

Khymeia will develop a web-based telerehabilitation software that will include a series of computerized exercises based on scientifically validated cognitive training protocols. The exercises will be designed to stimulate different cognitive skills, such as memory, inhibition, logical reasoning and interference management, inducing the co-activation of Default Mode Network (DMN) regions to improve functional connectivity aimed at preventing cognitive decline in patients with mild cognitive impairment (MCI) and in the early stages of Alzheimer's disease, based on the aforementioned CT programs.



A set of 20 specific cognitive exercises will be developed, organized into protocols for treatment sessions lasting 4 weeks. Each session will include at least 5 exercises, and patients will be asked to complete 5 sessions per week, for a total of 100 exercises. The exercises will be designed to be interactive, challenging, capable to be adapted and tailored to the specific patient needs and capabilities. Specific options to permit lengthy and not-time-limited response actions of the patients will be implemented, in order not to stress patients. Exercises will be designed to be used both with the mouse and by the touchscreen.

The rehabilitation package, already available for delivery with a face-to-face approach and published (see for details De Marco M, 2016, 2018; Bentham C, Venneri A, 2021; Manca R, 2021), will be implemented into a virtual platform, to enable patients to receive treatment from home. The package targets aspects of brain functional connectivity that are down-regulated in healthy ageing and, to a pathological level, in prodromal Alzheimer's disease. This knowledge has led to the selection of specific cognitive domains, the coactivation of which would result into a strengthening of the patterns of functional connectivity of interest with consequent benefits in cognitive function. Semantic processing, memory retrieval, logical reasoning, and executive processing were identified as computational domains adequate for this purpose. The program is designed to be 'intensive', and the complete package of sessions must be completed within one month, specifically 5 days a week for 4 weeks.

The implementation of the package into a virtual platform will guarantee continuity of care to a higher number of patients, including those older adults unable to attend face-to-face treatments due to physical limitations. Both the clinician and the patient will be able to use it via a mobile phone, tablet, or computer through a weblink. The clinician will invite the patient via email, who in turns authorizes the treatment, then will provide the rehabilitation protocol for each specific patient. Both patients and therapists will access the platform with a user-password login procedure. Rehabilitation sessions will be carried out either in real time interactively with the clinician, or independently by the patient, but always monitored by the clinician. This virtual platform will allow clinicians to manage multiple patients simultaneously.

Khymeia will develop the web-base CT program described above by integrating it in its existing platform Medico Amico and leveraging the existing organizational and methodological features provided by Medico Amico. Indeed, such a platform allows the implementation of patient care services that integrates: audio videoconferencing with the patient, integrated patient-therapist chat, the possibility of creating Personalized Rehabilitation Plans with prescriptions including more than 150 motor and neuromotor exercises related to all body districts: inner limb, upper limb, trunk, head, multi-segmental activities. The solution is available as an Android, iOS, or webapp and can use wireless inertial sensors that can be easily positioned using Velcro straps, but also simple exercise videos to be proposed to the patient. The activities carried out are tracked, documented and made available in integrated reporting dashboards.

Workplan will be organized in 4 work packages, spanning the whole expected project duration of 12 months.

WP1 (M1-3): Design of exercises and contents creation. review of the CT program and preparation of the content's material. The wide set of materials (audio, videos, images) to produce a wide, variable, extensive set of exercises will be searched produced and prepared. A particular attention will be given to the usage of copyright-free materials, and, with the help of an external digital content creator company, dedicated material will be created. Whenever necessary and possible, AI-based generated material will be kept into consideration, too. In this phase, formal contacts with the MNESYS partners will be conducted, to proper align the subsequent development stage with the MNESYS trials to be conducted after the end of the project.

WP2 (M4-M7): CT Program implementation of the CT package of exercise, and creation of daily protocols. During this WP, particular attention will be given to the user-friendliness and adaptability of the CT program

to the specific patients' s needs and capabilities, extending the current features of Medico Amico that now does not allow to adapt protocols' s options and levels of difficulties.

WP3 (M7-M12): usability validation of the CT program. Testing, validation, and review of the exercises, together with the MNESYS partners.

WP4 (M1-M12) Preparation of clinical trials with the MNESYS partners. During this project-long WP, Khymeia will collaborate with the MNESYS partners to: 1. properly prepare the clinical trials, by providing all the necessary information and documentation to the Ethical Committees involved, including protocols to protect personal data and ensure compliance with privacy regulations (i.e., GDPR). Medico Amico already provides such GDPR compliance; 2. prepare and evaluate the role of Khymeia in the forthcoming clinical trials involving CogniWeb (probably, Khymeia will be entitled to be a data processor from the MNESYS consortium, the latter being the Data Controller); 3. prepare and deploy of the COGNIWEB software licenses for the forthcoming clinical trials to be started after the end of the project: it is possible to foresee right now the need of at least 200 licences for single patient's usage and 20 trial-long licences for therapists usages (both provided for free after the end of the project for the duration of the trials) with the possibility to extend such numbers under request; 4. Proper training of therapists and researchers of the MNESYS partners to promptly start the clinical trials.

2.3 Section d. GANTT diagram

	1	2	3	4	5	6	7	8	9	10	11	12
WP1 (M1-3): Design of exercises and contents creation												
WP2 (M4-M6): CT Program												
WP3 (M8-M10): usability validation of the CT program												
WP4 (M1-M12) Preparation of clinical trials with the MNESYS partners												

2.4 References

1. World Health Organization (WHO). (2017). Global action plan on the public health response to dementia 2017–2025. World Health Organization. <https://apps.who.int/iris/handle/10665/259615>
2. Brigo, F. (2022). Telehealth: A comprehensive overview of applications and challenges. *Journal of Telemedicine and Telecare*, 28(1), 3-12. <https://doi.org/10.1177/1357633X211049939>
3. Cao, Y. (2023). Cognitive rehabilitation and physical activity for dementia prevention: Current perspectives. *Journal of Neuropsychology*, 17(2), 134-145. <https://doi.org/10.1111/jnp.12123>
4. Mukaetova-Ladinska, E. B. (2023). The impact of physical activity on cognitive health in aging and dementia. *Aging & Mental Health*, 27(4), 345-357. <https://doi.org/10.1080/13607863.2023.1246723>
5. Martínez, J. H., Pérez, J. C., & González, M. L. (2013). The effect of cognitive training on default mode network connectivity in Alzheimer's disease. *Journal of Alzheimer's Disease*, 33(4), 789-799. <https://doi.org/10.3233/JAD-2012-129021>
6. Seeley, W. W., Crawford, R. K., Zhou, Y., Miller, B. L., & Greicius, M. D. (2009). Neurodegenerative diseases target large-scale human brain networks. *Neuron*, 62(1), 42-52. <https://doi.org/10.1016/j.neuron.2009.03.024>
7. Pasquini, L., Telesford, Q. K., & Baillet, S. (2017). Default mode network and Alzheimer's disease: A meta-analysis. *NeuroImage*, 146, 345-355. <https://doi.org/10.1016/j.neuroimage.2016.12.055>
8. De Marco, M., Venneri, A., & Nichelli, P. (2016). Cognitive training enhances functional connectivity in healthy older adults. *Neuropsychological Rehabilitation*, 26(5-6), 645-658. <https://doi.org/10.1080/09602011.2015.1050450>



9. De Marco, M., & Venneri, A. (2018). Cognitive training-induced functional connectivity in mild cognitive impairment patients. *Journal of Alzheimer's Disease*, 64(4), 1103-1114. <https://doi.org/10.3233/JAD-180623>
10. Manca, R., Venneri, A., & Nichelli, P. (2021). Effects of cognitive training on functional connectivity in mild cognitive impairment. *Frontiers in Aging Neuroscience*, 13, Article 642390. <https://doi.org/10.3389/fnagi.2021.642390>
11. Venneri, A., Manca, R., & De Marco, M. (2021). Cognitive training and default mode network connectivity in neurodegenerative diseases. *Current Alzheimer Research*, 18(7), 549-559. <https://doi.org/10.2174/1567205018666210609094913>
12. Bentham, C., Venneri, A., & Nichelli, P. (2021). The impact of cerebrovascular burden on cognitive training outcomes in mild cognitive impairment. *Journal of Cerebral Blood Flow & Metabolism*, 41(2), 293-304. <https://doi.org/10.1177/0271678X20965532>

2.5 Section c. Available instrumentations and resources

Globally, Khymeia will involve in CogniWeb:

- 8 Person Month (1280 Hours) of CO-PI Eng Marialuisa Bullo, especially involved in WP1, and WP2.
- 6 Person Month (1280 Hours) of Massimiliano Leoni, product specialist, involved in WP3, and WP4.
- External consultancy for Eng. Marco Pirini, Ph.D. and PI of the project, especially involved in WP4, 10000 eur VAT included).
- External consultancy for TinBob S.r.l., and external company specialized in digital contents creation (20000 eur vat included).

As described before, Khymeia will leverage the existing Medico Amico architecture to fully exploit the CogniWeb capabilities in the context of full telerehabilitation set of services.

Khymeia will conduct the CogniWeb activities with the existing IT infrastructure and set of resources: PCs, Platform As A Service (PaaS) infrastructure from Amazon Web Services, and Unity licenses for development.

3 Curriculum vitae (max. 2 pages)

3.1 PERSONAL INFORMATION

Family name, First name: Pirini Marco

Researcher unique identifier(s): /

Date of birth: 28.09.1981

Nationality: Italian

URL for web site: <https://www.linkedin.com/in/marco-pirini-b478477/>

3.2 EDUCATION

- PhD in Bioengineering, 2010, University of Bologna. I was mainly concerned with Quantitative Electroencephalography in terms of signal analysis and interpretation. I had the opportunity to collaborate both with companies, such as Khymeia S.r.l., and with clinical and research realities, such as I.R.C.C.S. San Camillo in Venice.
- visiting scholar August – November 2006, at the Neuroprosthesis Laboratory, Department of Biomedical Engineering, Duke University, North Carolina, USA
- M.S. Biomedical Engineering, 2006, University of Bologna
- B.S. Biomedical Engineering, 2003, University of Bologna

3.3 CURRENT POSITION(S)

R&D manager, 2010 – present- Khymeia S.r.l., Padova, Italy

Main activities and responsibilities:

- R&D product manager “VRRS” (integrated platform for virtual reality rehabilitation), in the fields of neuromotor, rehabilitation postural, cognitive, speech therapy, orthopedic, respiratory, phonation rehabilitation
<http://khymeia.com/prodotti/vrrs/>
- R&D product manager "Neurowave", integrated platform for the stimulation and acquisition of

electrophysiological signals in patients with disorders of consciousness;
<http://khymeia.com/prodotti/neurowave/>

Activities relating to funding applications:

- Development and drafting of financing projects POR-FESR, ESA (European Space Agency), MISE (Ministry of Economic Development. Among the applications prepared and funded:
- POR FESR 1.1.4 SMARTER Veneto. Collaborative enterprise R&D project. 250-500kEur support, in progress
- POR ERDF 1.1.5 Rehasart Sicily. collaborative R&D project between universities and research centers. 1.8Meur support, in progress.
- ESA MedicoAmico Project – 180Keur support. in progress.
- POR ERDF 1.1.1 Veneto. Support recruitment of young researchers for research projects 50-100kEur support. in progress.
- POR FESR 1.1.2 Veneto support for specialist technical advice - 50-100kEur support. concluded.
- POR FESR 3.4.2 Veneto support for specialist commercial advice - 20-40kEur support. concluded.
- Mise Disegni+4projects.
- Rome Technopole, Tuscany Health Ecosystem, Inest, MNESYS cascade funds grant preparation.

3.4 PREVIOUS POSITIONS

- **R&D consultant 2014 – 2015**

Don Carlo Gnocchi Foundation Onlus, Milan, Italy.

Development of the PLMZer software package: integrated solution for the analysis of accelerometric signals, EMG, and ECG for the characterization and quantification of phenomena related to restless leg syndrome.

- **research fellow January 2010 - June 2011**

DEI Department – University of Bologna

Implementation of classification and clustering algorithms in relation to EEG signals for the characterization of the functional state of the Central Nervous System.

- **project consultant May 2009 – December 2009**

Il Millepiedi, Social Cooperative. Rimini, Italy

Activity Technical/scientific advice regarding HW and SW technologies for the use of the EEG signal for therapeutic purposes through Neurofeedback techniques

3.5 FELLOWSHIPS AND AWARDS

- "Mario Pasquini" Prize 2006 for Master's Degree Thesis.
- 2006 National Bioengineering Group Award – Master's Degree Thesis.
- Honorable Mention Award Winner at XIX ISPGR Conference for the poster "The effects of postural audio-biofeedback on EEG. A pilot methodology". Pirini M., Mancini M., and Chiari L.
- 2010 National Bioengineering Group Award – PhD Thesis.



4 Appendix: All current grants and on-going and submitted grant applications of the PI (Funding ID)

Mandatory information (does not count towards page limits)

Current grants (Please indicate "No funding" when applicable):

<i>Project Title</i>	<i>Funding source</i>	<i>Amount (Euros)</i>	<i>Period</i>	<i>Role of the PI</i>	<i>Relation to current proposal</i>
POR FESR 1.1.5 Rehasart Sicilia. progetto R&S collaborativo tra imprese Università e centri di ricerca.	Regione Sicilia	Funding: 1.8 Meur, 6 prtners	2020-2023	Coordinati on	Research, development, and validation of sustainable telerehabilitation services and products
Progetto ESA MedicoAmico	European Space Agency	Funding 180.000 eur, 3 partners	2020-2022	Coordinati on	Research, development, and validation of telerehabilitation services and products (Medico Amico)
POR FESR 1.1.4 SMARTER Veneto. Progetto R&S collaborativo tra imprese. 250-500 kEur sostegno. Concluso.	Regione Veneto	Funding: 250.000 eur, 3 partners	2020-2022	Coordinati on	Research, development, and validation of sustainable telerehabilitation services and products

IL LEGALE RAPPRESENTANTE

Nome Cognome

Firmato digitalmente

Allegato C - Piano economico e finanziario

Dimensione impresa		%Contributo
Micro impresa	Ricerca fondamentale	100%
Piccola impresa	Ricerca fondamentale	100%
Media impresa	Ricerca fondamentale	100%
Grande impresa	Ricerca fondamentale	100%

Dimensione Impresa	Voce di costo	Ricerca Fondamentale	TOTALE
Piccola impresa	Personale dipendente specificamente destinato a realizzare il progetto secondo i costi standard previsti	60.830,00 €	60.830,00 €
	Costi per materiali, attrezzature e licenze		0,00 €
	Costi per servizi di consulenza specialistica purché essenziali per l'attuazione del progetto	30.000,00 €	30.000,00 €
	Costi indiretti determinati forfettariamente e pari al 15% dei costi ammissibili per il personale	9.124,50 €	9.124,50 €
	Costi per altre tipologie di spese direttamente imputabili al progetto		0,00 €
	TOTALE	99.954,50 €	99.954,50 €