UNIVERSITÀ DEGLI STUDI DI GENOVA

AREA RICERCA, TRASFERIMENTO TECNOLOGICO E TERZA MISSIONE

SERVIZIO PER IL TRASFERIMENTO TECNOLOGICO E DELLE CONOSCENZE

SETTORE VALORIZZAZIONE DELLA RICERCA, TRASFERIMENTO TECNOLOGICO E RAPPORTI CON LE IMPRESE

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;

VISTA la delibera della seduta del 27 settembre 2023 con cui il Consiglio di Amministrazione dell'Università degli Studi di Genova ha approvato l'emanazione del bando a cascata per organismi di ricerca nell'ambito del Progetto MNESYS - "*A multiscale integrated approach to the study of the nervous system in health and disease* - PNRR M4C2 per lo Spoke 6;

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

del Procedimento;

VISTO il Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 di emanazione del Bando a cascata per il finanziamento di proposte di intervento per le attività di ricerca svolte da Organismi di Ricerca nell'ambito del programma di ricerca PE 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);

CONSIDERATO che alla data di scadenza per la presentazione delle proposte progettuali, fissata entro e non oltre il giorno 14 dicembre 2023, per la **Tematica M – "Integrated approaches of molecular imaging, quantitative magnetic resonance imaging, and radiomics to characterize heterogeneity in neurodegenerative diseases"** era pervenuta a mezzo PEC all'indirizzo air3@pec.unige.it la seguente proposta:

PROPONENTE: Università degli Studi di Roma "La Sapienza"
TITOLO PROPOSTA: SleepAD – Integrated Multi-parametric Imaging, Neurophysiological Biomarkers, and Artificial Intelligence to Study the Relationships Among Sleep Disorders, Glymphatic System Dysfunctions, Brain Amyloidosis and Connectivity, and Epileptiform Activity in Prodromal Alzheimer's Disease

TENUTO CONTO che la Responsabile del procedimento, Ing. Patrizia Cepollina, ha ritenuto ricevibile, ammissibile e conforme la proposta sopra citata;

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. 6114 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 l'Estratto del Verbale della Riunione del 12 febbraio 2024 del Comitato Scientifico del programma di ricerca MNESYS "*A multiscale integrated approach to the study of the nervous system in health and disease*" che ha approvato la "Rosa di Candidati" per le Commissioni di Valutazione dei Bandi a cascata sul Programma MNESYS;

VISTO il Decreto del Rettore n. 855 del 20 febbraio 2024 con cui è costituito l'Albo a supporto delle valutazioni 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 "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS, a valere sulle risorse del Piano Nazionale di Ripresa e Resilienza (PNRR), Missione 4 "Istruzione e Ricerca", Componente 2 "Dalla ricerca all'impresa", linea di Investimento 1.3 "Creazione di Partenariati Estesi alle università, centri di ricerca, alle aziende per il finanziamento di progetti di

ricerca di base";

VISTO il Decreto del Rettore n. 1124 del 5 marzo 2024 con cui è stata nominata la Commissione di valutazione delle proposte pervenute in risposta al bando a cascata di cui al D.R. n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

ACQUISITO il verbale della Commissione di Valutazione della seduta del 16 aprile 2024 (Prot. n. 37982 del 07/05/2024);

VISTO il Decreto del Rettore n. 2294 del 10 maggio 2024 con cui è stata approvata la graduatoria di merito per la Tematica M – "Integrated approaches of molecular imaging, quantitative magnetic resonance imaging, and radiomics to characterize heterogeneity in neurodegenerative diseases", di cui al bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

TENUTO CONTO che in data 14 maggio 2024 è stata inviata all'Università degli Studi di Roma "La Sapienza" la comunicazione con prot. n. 41372 in cui si rendevano noti gli esiti della procedura e si richiedeva la documentazione propedeutica all'adozione del provvedimento di ammissione del finanziamento;

VISTO che in data 27 maggio 2024 con prot. n. 46827 la documentazione richiesta è stata ricevuta dall'Università degli Studi di Genova che l'ha ritenuta conforme a quanto previsto nel bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 , indicato nelle premesse del presente decreto,

DECRETA

ART. 1

L'ammissione a finanziamento del progetto SleepAD – Integrated Multi-parametric Imaging, Neurophysiological Biomarkers, and Artificial Intelligence to Study the Relationships Among Sleep Disorders, Glymphatic System Dysfunctions, Brain Amyloidosis and Connectivity, and Epileptiform Activity in Prodromal Alzheimer's Disease per la **Tematica M – "Integrated approaches of molecular imaging, quantitative magnetic resonance imaging, and radiomics to characterize heterogeneity in neurodegenerative diseases"** con Soggetto proponente l'Università degli Studi di Roma "La Sapienza" – come rappresentato negli Allegati B e C alla proposta presentata con domanda di partecipazione prot. n. 74345 del 13 dicembre 2023.

ART. 2

L'entità dell'agevolazione concessa, a fondo perduto, ammonta a 149.683,25 euro complessivi come rappresentati nell'allegato C alla proposta presentata con domanda di partecipazione prot n. 74345 del 13 dicembre 2023. L'agevolazione è pari al 100% dei costi di progetto trattandosi di attività di ricerca fondamentale per Organismi di Ricerca. L'agevolazione è concessa a valere sui fondi PNRR - Programma "*A multiscale integrated approach to the study of the nervous system in health and disease*" – MNESYS Codice PE00000006 a valere sulla Missione 4, Componente 2, Investimento 1.3, ai

sensi del Decreto di concessione n. 1553 dell'11 ottobre 2022, registrato alla Corte dei Conti il 23/11/2022 n. 2948, iscritto al Bilancio di Ateneo sul progetto UGOV 100009-2022-TF-PNRR-PE_MNESYS_BAC_DINOGMI.

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 12 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

(m) Integrated approaches of molecular imaging, quantitative magnetic resonance imaging, and radiomics to characterize heterogeneity in neurodegenerative diseases

Project Title (Acronym)

Integrated Multi-parametric Imaging, Neurophysiological Biomarkers, and Artificial Intelligence to Study the Relationships Among Sleep Disorders, Glymphatic System Dysfunctions, Brain Amyloidosis and Connectivity, and Epileptiform Activity in Prodromal Alzheimer's Disease (SleepAD)

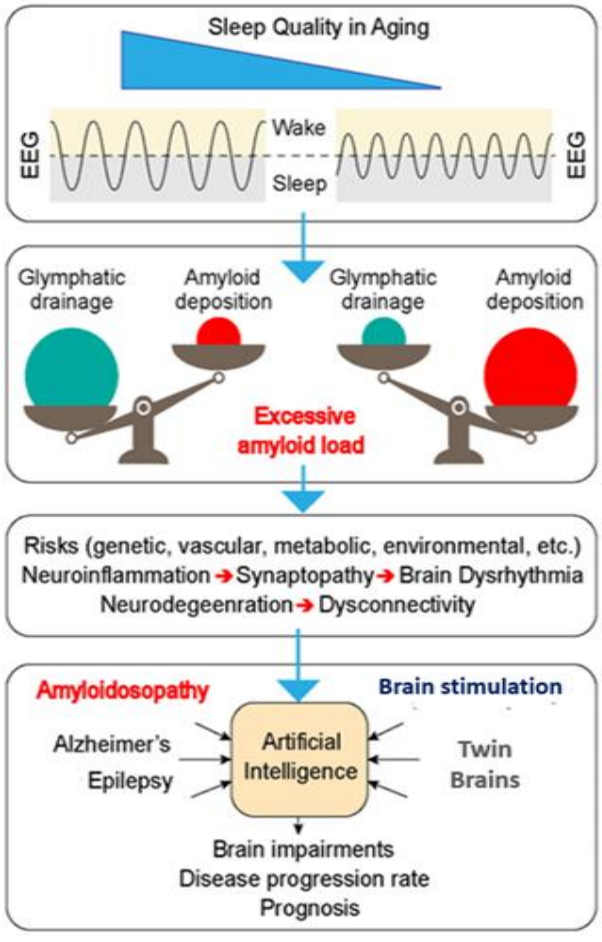
- Name of the PIs' host institution for the project: **Department of Physiology and Pharmacology "Erspamer," Sapienza University of Rome**
- Name of the Principal Investigator (PI): **Prof. Claudio Babiloni**
- Proposal duration in months: **12**
- Financing required: **149,683.25 Euro**

- Name and qualification of the Principal Investigator (PI)
- Name and qualification of the co-principal Investigator (PI)
- Name and qualification of the components of the research team:

ROLE IN THE PROJECT	*NAME*	*SURNAME*	*DEPARTMENT*	*QUALIFICATION*	*YOUNG (under 40 al 31.12.2023)*	*F/M*
Principal Investigator	*Claudio*	*Babiloni*	*Physiology and Pharmacology "V. Erspamer"*	*Full Professor of Physiology*		*M*
co-Principal Investigator (PI)	*Claudio*	*Del Percio*	*Physiology and Pharmacology "V. Erspamer"*	*Associate Professor of Physiology*		*M*
Expert of Physiology	*Eleonora*	*Palma*	*Physiology and Pharmacology "V. Erspamer"*	*Full Professor of Physiology*		*F*
Neurologist	*Paolo*	*Onorati*	*Physiology and Pharmacology "V. Erspamer"*	*Researcher*		*M*
Neurologist	*Franco*	*Giubilei*	*Neurosciences, Mental Health, and Sense Organs*	*Associate Professor of Neurology*		*M*
Expert of Neuroimaging	*Patrizia*	*Pantano*	*Human Neurosciences*	*Full Professor of Radiology*		*F*
Expert of Neuroimaging	*Filippo*	*Carducci*	*Physiology and Pharmacology "V. Erspamer"*	*Technologist*		*M*
Expert of Neuroimaging	*Claudia*	*Piervincenzi*	*Human Neurosciences*	*Researcher-RTDA*	*< 40 ys*	*F*
Neurologist	*Fabrizia*	*D'Antoni*	*Human Neurosciences*	*Researcher-RTDA*	*< 40 ys*	*F*
Expert of EEG	*Roberta*	*Lizio*	*Physiology and Pharmacology "V. Erspamer"*	*Researcher-RTDA*		*F*
Expert of EEG	*Susanna*	*Lopez*	*Physiology and Pharmacology "V. Erspamer"*	*Contract for Research*	*< 40 ys*	*F*
Psychologist	*Matteo*	*Carpi*	*Human Neurosciences*	*Ph.D. fellow*	*< 40 ys*	*M*
Psychologist	*Giulia*	*Cartocci*	*Molecular Medicine*	*Researcher-RTDA*	*< 40 ys*	*F*

ABSTRACT

AIM. Sleep disorders and brain amyloidosis may sway the onset and the course of Alzheimer's (AD). However, the mechanistic links remain elusive. This proposal aims to test the hypothesis that measures of sleep quality, glymphatic system function, brain amyloidosis, and disease risk-resilience factors (e.g., genetics, lifestyle, environment, and their comorbidities) as an input to ***artificial intelligence*** – machine learning (AI) tools may ***predict*** brain structural-functional abnormalities (e.g., grey matter atrophy, cerebrovascular lesions, cortical functional connectivity, and excitatory/inhibitory balance triggering epileptiform activity and vigilance dysregulations) and clinical status in AD patients with mild cognitive impairment (ADMCI). The concept of the project is illustrated in the following graphic abstract.
DESIGN. To this aim, we will synergistically conduct ***retrospective*** longitudinal (1- and 2-year follow-ups; FP7-IMI-PharmaCog project database available at https://www.neugrid2.eu/index.php/datasets/) and prospective cross-sectional (proof-of-concept) clinical studies in ***ADMCI*** patients. Clinical, digital, and EEG data will measure disease ***risks***, cognition, ***wake-sleep*** functions, and cortical excitability (e.g., ***epileptiform*** activity). Cerebrospinal fluid biomarkers will measure brain neuropathology, including ***amyloidosis***. Magnetic resonance imaging will probe brain ***glymphatic*** function, ***neurodegeneration***, vascular lesions, and functional ***connectivity***. Data features will be input into combined AI tools to test the working hypotheses. Results may produce mechanistic insights into ***prodromal AD*** and risk-resilience factors through AI models, validating ***biomarkers*** and unveiling ***new targets*** for prevention, clinical decision-making, and intervention.



GRAPHICAL ABSTRACT. *Schematic illustration of the **concept** and core procedures for testing the critical premise of the project. From top to bottom: (1) associated with the aging decline, reduced quality of non-rapid eye movement (NREM) **sleep** attenuates the **glymphatic** drainage, promotes the build-up of **amyloids** in the brain, and triggers other pathological processes related to **Alzheimer's disease** (AD). In interaction with AD **risk factors** (e.g., genetics, age, sex, education attainment, cerebrovascular, diet, sedentariness, inflammation, synaptic impairments, environmental, etc.), these pathological processes may induce the breakdown of brain connectivity and cognitive decline and lead to mild cognitive impairment (MCI) and dementia due to AD. Using **artificial intelligence** – machine learning (AI) tools and experimental data from ADMCI patients, this research proposal aims to develop models to support clinical decision-making, predict patients' cognitive status, and guide interventions. To this aim, we will conduct a **retrospective** longitudinal study using the clinical, cerebrospinal fluid (Abeta42/40, phospho tau, total tau, etc.), neuroimaging (structural, diffusion, and resting-state functional magnetic resonance imaging), and EEG data collected at baseline, 1-year, and 2-year-follow ups in **ADMCI and control patients** during the FP7-IMI project entitled "**PharmaCog**," granted by European Committee (2010-2015). In that "PharmaCog" project, the principal investigator of the present proposal (Prof. Claudio Babiloni) played the role of **EEG data Leader** and has already formally obtained permission from the PharmaCog Ethical Committee (September 26, 2023) to use the whole "PharmaCog" multimodal clinical trial database available at the open-science service "**neuGRID2**" (https://www.neugrid2.eu/index.php/datasets/). Furthermore, a **prospective** "proof-of-concept" multimodal (clinical, CSF, MRI, and EEG) study in ADMCI patients will be performed at UNIROMA1 to **cross-validate** the results.*

RESEARCH PROPOSAL

Sections (a) and (b) should not exceed 4 pages. References do not count towards the page limits.

SECTION A. STATE-OF-THE-ART AND OBJECTIVES

THE SOCIETAL CHALLENGE OF THE ALZHEIMER'S DISEASE (AD). According to the World Alzheimer Report 2018 (https://www.alzint.org/resource/world-alzheimer-report-2018/), aging is the primary risk factor for neurodegenerative diseases (NDDs) belonging to severe cognitive deficits and disabilities in the activity of daily living (dementia). The most common NDD, ***Alzheimer's disease*** (AD), affects about ***30 million*** people worldwide, with a projected increase to about 60 million by 2050. Unfortunately, AD is neither fully understood nor can be stopped by medications until now. As a result, global ***annual costs*** related to AD are about US ***1 $ trillion*** and are expected to surpass about 1.5 $ trillion by 2030. AD is characterized by an age-dependent buildup of misfolded proteins, manifested by extracellular deposits of ***amyloid-beta*** plaques and intra-neuronal inclusions of misfolded phospho tau (p-tau). The buildup of these proteins in the brain triggers neuroinflammation and toxicity, leading to a breakdown of synaptic connections and loss of neurons and glial cells. In old persons with intact cognition, the presence of ***Alzheimer's-like amyloidosis*** may induce rapid clinical deterioration in relation to unmodifiable (e.g., genetic) and modifiable ***risk factors*** (e.g., diet, physical exercise, sleep, cognitive training, environmental factors, etc.).

THE SLEEP, GLYMPHATIC SYSTEM, AND BRAIN AMYLOIDOSIS. The buildup of amyloid-beta plaques with intracellular inclusions of p-tau in the brain has been viewed mainly in association with their abnormal processing and degradation (Tarasoff-Conway et al., 2015). The increase in levels of soluble amyloids has been shown to trigger nucleation, attracting other species of amyloid proteins and forming lesions and vascular deposits (Tornquist et al., 2018; Cohen et al., 2013, 2018). This process is influenced by multiple factors, including the conformation and concentration of proteins and fragments, the ionic strength of the environment with local pH, and a favorable physical interface for seeding and aggregation (Soto and Pritzkow, 2018; Chiti and Dobson, 2017; Bah et al., 2023).
The role of fluid phase mobility in the onset of amyloidosis has recently been reported, with the stagnation of proteins and their misfolded fragments in interstitial space promoting the process (Boespflug and Iliff, 2018; Benveniste et al., 2019). This mechanism attracted much interest after discovering the critical role of the brain's ***glymphatic system*** in controlling the flow of interstitial fluid with toxin and metabolite clearance through a unique set of perivascular channels and conduits formed by astroglia cells (Iliff et al., 2012; Hablitz and Nedergaard, 2021; Jessen et al., 2015; Nedergaard and Goldman, 2020). Notably, glymphatic clearance is very active during deep stages of ***non-rapid eye movement (NREM)*** sleep and declines dramatically with sleep impairments, causing disruptions in brain homeostasis with toxicity and the buildup of toxic levels of amyloids (Iliff et al., 2012; Hablitz and Nedergaard, 2021; Jessen et al., 2015; Nedergaard and Goldman, 2020). In complex with a weight of ***AD risks*** (e.g., genetic, age, sex, education attainment, diet, sedentariness, metabolic, cardiovascular, trauma, socioeconomic, environmental, and other factors), sleep disorders and the failure of the above homeostatic process leads to detrimental effects on brain mechanisms and functions (Mullane et al., 2018). However, there is a critical knowledge gap in how disrupted sleep with impaired glymphatic activity through interplay with brain amyloidosis and those risks may predict the clinical manifestation of AD and its course (Mullane et al., 2018).
Among other pathological effects, AD-related brain amyloidosis may induce overexcitability in patients' cerebral cortex, with subclinical and clinical epileptiform activity revealed by eyes-closed resting-state ***electroencephalographic*** (rsEEG) recordings probing the neurophysiological systems regulating ***quiet vigilance*** and transitions to ***sleep***: (1) in AD, the incidence of convulsive seizures is 10 times higher than in the age-matched general population (Horváth et al., 2016); (2) epilepsy is 87 times more frequent in AD patients with early- than late-onset disease (Scarmeas et al., 2009); (3) cognitive decline starts 5.5 years earlier in AD patients with epilepsy than in AD without epilepsy (Vossel et al., 2013); (4) periodic EEG abnormalities have been described in AD and seniors with non-convulsive status epilepticus (Minkeviciene et al., 2009); (5)

subclinical epileptiform activity accelerated the progression in ADMCI patients in a 3-year-long prospective follow-up study (Horváth et al., 2021); (6) pharmacological interventions with anti-epilepsy symptomatic treatments (e.g., Levetiracetam) had some beneficial effects on cognitive functions in AD patients with epileptiform activity (Picco et al., 2011; Vossel et al., 2021; Hautecloque-Raysz et al., 2023).

PREVIOUS JOINT SCIENTIFIC PUBLICATIONS OF THE PROPONENTS ON THE CALL TOPIC, MOSTLY IN COOPERATION WITH THE PE#12-SPOKE#6 UNIGE WORKGROUP. In the past two decades, the proponents and the PE#12-Spoke#6 Neurodegenerative Disease Workgroup of UNIGE (formerly, Dr. Guido Rodriguez and Dr. Flavio Nobili; Dr. Dario Arnaldi, Francesco Famà, Andre Brugnolo, Nicola Girtler, Silvia Morbelli, etc.) have intensively cooperated to validate positron emission tomography (PET), magnetic resonance imaging (MRI), and rsEEG source biomarkers of molecular, structural, and functional abnormalities in patients with AD and related disorders, as a methodological and a conceptual basis of the present research proposal. Most of the following results of the proponent group were grounded on such scientific cooperation (see the following references with ***Claudio Babiloni*** and ***Flavio Nobili*** as co-authors):
(1) Posterior rsEEG delta (< 4 Hz) and alpha (8-10 Hz) source activity and connectivity were correlated with the atrophy of the hippocampal and global cortical gray matter (Babiloni et al., 2009a, 2013, 2015), the impairment of the tract from the cholinergic basal forebrain to cerebral cortex (Babiloni et al., 2009b, 2010), and subcortical vascular lesions (Babiloni et al., 2006, 2008, 2011) in ADMCI and ADD patients, as measured by structural MRIs.
(2) Widespread rsEEG delta source activity was correlated to cortical hypometabolism in ADD patients, as measured by FDG-PET (Babiloni et al., 2016).
(3) Posterior rsEEG delta and alpha source activity was correlated with the cortical functional connectivity in ADMCI and ADD patients, as measured by resting-state functional MRI (rs-fMRI, Galluzzi et al., 2016; Brueggen et al., 2017; Jovicich et al., 2019; Babiloni et al., 2023).
(4) Posterior rsEEG delta, theta (4-7 Hz), and alpha source activity and connectivity mostly discriminated with accuracy > 80% individuals with ADMCI and ADD patients over healthy controls and patients with MCI and dementia due to Parkinson's and Lewy body diseases; ROC curves obtained this accuracy (Babiloni et al., 2017a, 2017b, 2018a, 2018b, 2019) and AI tools using support vector machines (San-Martin et al., 2021) and artificial neural networks (Rossini et al., 2008; Triggiani et al., 2017; Ferri et al., 2021).
Furthermore, the proponent group and the experts of the UNIGE Workgroup cooperated into three international expert panels of the Alzheimer's Association (Babiloni et al., 2020, 2021) and European Neuroscientific Societies (Festari et al., 2023) to review the literature on the rsEEG biomarkers in AD. Two of those panels recommended more investments and research on the rsEEG biomarkers reflecting abnormal cortical neural oscillatory synchronization mechanisms in AD patients, sensitive to the disease course, possibly related to the altered regulation of vigilance in wakefulness and quality of life (Babiloni et al., 2020, 2021). Notably, those rsEEG rhythms may be easily obtained. The third expert panel (Festari et al., 2023) recommended the use of rsEEG biomarkers when there is diagnostic suspect that MCI and dementia may be due to subclinical epileptiform waveforms even in AD patients without a clinical diagnosis of epilepsy (Babiloni et al., 2022).

AIM OF THE SleepAD PROJECT. In summary, sleep disorders and brain amyloidosis may sway the onset and the course of Alzheimer's (AD). However, the mechanistic links remain elusive. This project aims to test the hypothesis that combined measures of sleep quality, glymphatic system function, brain amyloidosis, and disease risk-resilience factors (e.g., genetics, lifestyle, environment, and their comorbidities) as an input to combined AI tools may predict brain molecular and structural-functional abnormalities (e.g., grey matter atrophy, cerebrovascular lesions, cortical functional dysconnectivity, and excitatory/inhibitory imbalance triggering epileptiform activity and vigilance dysregulations) and clinical status and progression in ADMCI patients. Results may produce mechanistic insights into neurodegenerative dementing and risk-resilience factors, focusing on the effects of sleep disorders through combined AI models. Furthermore, the development of a validated multimodal biomarker panel enriched with the sleep quality-glymphatic system dysfunction-brain amyloidosis and connectivity dimensions could be of interest to support future clinical decision-making,

new prevention strategies, and future therapies for the identification of ADMCI individuals at higher risk of quickly progressing to dementia.
The ***SleepAD*** project may contribute to a true multiscale and multimodal approach to the study of the AD model in the ***MNESYS project*** frame of ***Precision Medicine***. The hypothesized relationships between ***sleep disorders***, ***glymphatic*** system dysfunctions, brain ***amyloidosis***, and ***epileptiform*** activity in combination with specific disease risk factors may guide (1) early preventive and personalized interventions and (2) new drug discovery pathways. The SleepAD project may also contribute to the ***MNESYS project's mission*** to promote the ***integration*** of medical (AD), biological (amyloidosis), technological (sleep telemonitoring), and computational (glymphatic system - AI tools) expertise to contrast a challenging disease of an aging society.

SECTION B. METHODOLOGY

DESIGN. To this aim, we propose the development of retrospective longitudinal and proof-of-concept prospective, cross-sectional clinical studies. The concept of the study design is illustrated in ***Figure 1***.
The ***retrospective longitudinal*** study will use the data collected in amnesic MCI patients during the Work Package 5 (WP5) of the FP7-IMI project entitled "PharmaCog," granted by the European Committee (2010-2015; https://cordis.europa.eu/project/id/115009). In the "PharmaCog" project, the principal investigator of the present proposal (Prof. Claudio Babiloni) played the role of EEG data Leader and has already formally obtained permission from the PharmaCog Ethical Committee (September 26, 2023) to use the whole "PharmaCog" multimodal clinical trial database available at the open-science service "neuGRID2" (https://www.neugrid2.eu/index.php/datasets/).
The detailed protocols of data collection and analysis of the PharmaCog datasets were finely reported in the reference project papers (Galluzzi et al., 2016; Marizzoni et al., 2019; Jovicich et al., 2019) and are just sketched in the following. In the WP5, 144 amnesic MCI patients (81 ADMCI and 63 noADMCI) received clinical and neuropsychological evaluation, cerebrospinal (CSF) and blood plasma biofluid (ApoE genetic, Abeta42/40, phospho tau, total tau, neurogranin, etc.), structural, diffusion, functional MRI, and rsEEG data recordings at baseline and five 6-month follow-ups (Galluzzi et al., 2016; Marizzoni et al., 2019; Jovicich et al., 2019). These findings represent the first longitudinal characterization of functional biomarkers of prodromal AD relative to "negative" aMCI patients based on so many serial recording sessions over 2 years. The best composite matrix discriminating the two MCI groups over 2 years included the MRI volumes of the hippocampal dentate gyrus and lateral ventricle, reduced rs-fMRI connectivity in the default mode network (DMN), abnormal posterior rsEEG delta and alpha sources (Galluzzi et al., 2016; Marizzoni et al., 2019; Jovicich et al., 2019).
In the ***present proposal***, the following ***new and original*** data analysis will be performed: (1) the evaluation of the sleep disorders from the clinical scales; (2) an analysis of DTI-ALP to index the glymphatic system dysfunction and correlate it with the CSF measures of Abeta42/40 and p-tau; (3) the rating of the eventual epileptiform activity in the serial rsEEG recordings; and (4) the estimation of rsEEG delta and alpha source activity and connectivity within and between the nodes of DMN and the correlation with the rs-fMRI connectivity measures between the DMN nodes. These data features and measures of genetic (ApoE), demographic (age, sex), and other (cerebrovascular, diet, sedentariness, socioeconomic, etc.) risk factors will be used as input for (1) the classification between ADMCI and noADMCI groups and (2) the prediction of the cognitive decline to 1-year and 2-year follow-ups based on four independent AI tools, such as Simple Logistic Regression Model Trees (Friedman et al., 2000), Logistic Regression (Yu et al., 2011), K-Nearest Neighbor (Bishop, 2006), and Support Vector Machine (Chang and Lin, 2011). The output performances of the four AI tools will be averaged as an index of prediction accuracy. The target cognitive status ("stable" vs. "decliner") of the MCI individuals at the follow-ups will be probed by the mini-mental state evaluation (MMSE) score.

The ***prospective cross-sectional*** study (proof-of-concept) will be performed on ADMCI patients at UNIROMA1 to extend the results of the retrospective study. The general methodology of the clinical, CSF, blood, MRI, and EEG data collection and the biomarker extraction will follow that of the "PharmaCog" WP5 clinical trial (Galluzzi et al., 2016; Marizzoni et al., 2019; Jovicich et al., 2019).

Using the published results of the PharmaCog project (Galluzzi et al., 2016; Marizzoni et al., 2019; Jovicich et al., 2019), the ***power analysis*** with $p < 0.05$ and 0.8 of desired power gave a ***sample size*** of N = 30, considering the single recording session planned.
Notably, the data clinical, MRI, and rsEEG data collection and analysis will extend that of the PharmaCog project by focusing on a careful evaluation of ***sleep quality*** and wake-sleep cycle through clinical, digital (actigraphy in telemonitoring), and EEG recordings. These fine measures will be correlated with the DTI-ALP ***glymphatic dysfunction***, brain ***amyloidosis***, risk of epileptiform activity, and several other disease ***risk factors*** (e.g., ApoE, age, sex, education attainment, cerebrovascular and metabolic, diet, sedentariness, socioeconomic, environmental, green space, etc.) to predict patients' brain functional dysconnectivity from rsEEG sources and rs-fMRI within and between the DMN nodes and the clinical status as measured by the MMSE score.

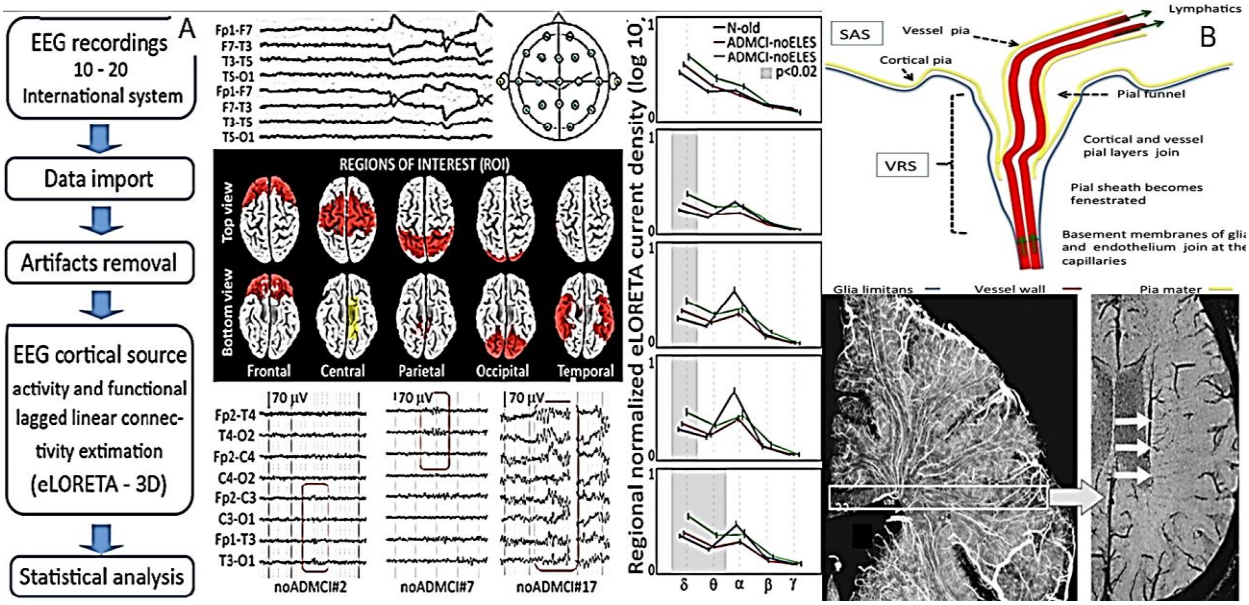


Figure 1. *(**A. Left-Middle**) Flow chart of the protocol for collection and eLORETA source analysis of EEG data from Alzheimer's disease mild cognitive impairment (ADMCI) patients and controls. An example of EEG traces from 10-20 scalp electrode montage and the schematized cortical regions of interest (inset with brain maps) of the eLORETA freeware for estimating EEG cortical source activity and connectivity. Under the maps, see typical EEG traces showing epileptiform signatures in 3 ADMCI patients with poor executive functions. Right to the maps, see widespread dominant eLORETA delta and temporal theta source activities in ADMCI patients with (green) over without (red) epileptiform activity; healthy control seniors as a reference (blue). (**B. Right**) Schematic diagram of Virchow-Robin space (VRS) or perivascular space delineated by glia, pia, and endothelium basal membranes. The VRS corresponds to the space surrounding vessels penetrating the parenchyma. The VRS is obliterated at the capillaries, where the basement membranes of the glia and the capillary endothelium join. The invagination of both cortical and vessel pia into the VRS makes a pial funnel. The pial sheath around arteries extends into the VRS but becomes more fenestrated and eventually disappears at the precapillary section of the vessel. Unlike arteries, veins do not possess a pial sheath inside the VRS. Interstitial fluid may drain through an intramural pathway along the basement membranes of capillaries and arterioles into the lymphatics (green arrows). SAS, subarachnoid space. The concept of the DTI-ALPS (diffusion tensor image analysis along the perivascular space) MRI method. In the white matter outside the lateral ventricular body, the medullary vessels run in the left-right direction (the MRIs in the bottom), the projection fibers in the vertical direction, and the association fibers in the anteroposterior direction.*

WP No.	Work Package (WP) Title	Leader	Start	End	Activity Type – Milestone/Deliverable
WP1	Coordination, Management, Dissemination and Communications	Babiloni C	1 m	12 m	Management – Reporting, Dissemination, Project Paper publication, and Alzheimer's Association Posters (12 m)
WP2	Retrospective longitudinal study on multimodal PharmaCog database	Giubilei F	1 m	9 m	RTD – Report on results (12 m)
WP3	Prospective cross-sectional study on multimodal SleepAD database	Del Percio C	1 m	12 m	RTD – Report on ethical clearance (3 m), platform (6 m), and results (12 m)
WP4	Translational AI tool models	Babiloni C	1 m	12 m	RTD – Report on the AI methods (6 m) and results (12 m)

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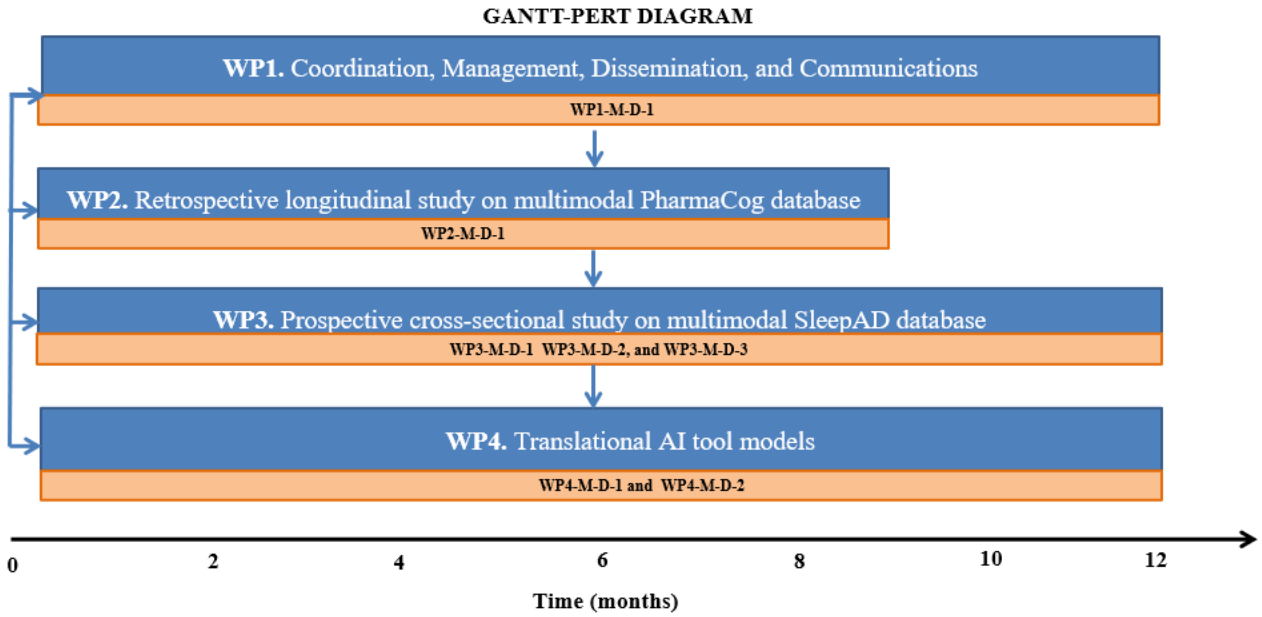
SECTION C. AVAILABLE INSTRUMENTATIONS AND RESOURCES

Workgroup of the Sapienza University of Rome (UNIROME1)	
General Description	**UniRoma1** is known as Sapienza University of Rome and is the largest European university (112,000 students, 4,000 professors/lecturers, 270 Academic Courses, 80 Doctorate Schools, 80 Resident Courses) and one of the oldest in history (founded in 1303). It has been directly involved in key changes and developments in Italian society.
Role and Commitment of Key Persons	**Prof. Claudio Babiloni** (male), 15%FTE commitment), Ph.D. (Biomedical Sciences) is a tenured Full Professor (Physiology). He is a neurophysiologist with an interest in EEG-EMG-EKG and neuroimaging biomarkers of neurodegenerative disorders and cognitive decline/frailty in seniors. Currently supervising 4 PhD students with 10 completions. He has a long experience in recording, analysis, and correlation of electroencephalographic (qEEG), clinical, neuropsychological, genomic, proteomic, bioinformatics, transcranial magnetic stimulation (TMS), structural and functional neuroimaging (MRI, fMRI) data in healthy subjects and neurological patients with cognitive deficits. He has published 7 book chapters and more than 300 peer-reviewed international papers (Scopus H index: 72). **Prof. Ing. Claudio Del Percio** (male), 15%FTE commitment), Ph.D. (Neurophysiology) is a tenured Associate Professor (Physiology). He is a neurophysiologist and new technologies (Artificial Intelligence-AI-machine learning tools) with an interest in EEG-EMG-EKG and neuroimaging biomarkers of neurodegenerative disorders and cognitive decline/frailty in seniors. Currently supervising 1 PhD student with 2 completions. He has a long experience in recording, analyzing, and using AI tools with inputs taken from electroencephalographic (qEEG), clinical, structural, and functional neuroimaging (MRI, fMRI) data in healthy subjects and neurological patients with cognitive deficits. He has published more than 130 peer-reviewed international papers (Scopus H index: 46). **Prof. Franco Giubilei** (male), 10%FTE commitment), Ph.D. (Neurophysiology) is a tenured Associate Professor (Neurology). He is a neurologist and Head of the Memory Clinic – Neurology Unit at the UNIROMA1 General Hospital S. Andrea. Currently supervising 1 PhD student with 6 completions. He has a long experience in clinical assessment and management of neurological patients with cognitive deficits. He has published more than 120 peer-reviewed international papers (Scopus H index: 37). **Susanna Lopez** (female, 15% commitment), Biomedical Engineer, PhD (Neurophysiology), is an expert in recording, analysis, and correlation of clinical, neuropsychological, qEEG, genomic, proteomic, bioinformatics, TMS, and structural MRI data in healthy subjects, neurological patients with cognitive deficits, as well as in preclinical models (mice). She has published 40 scientific papers (Scopus H index: 15).
Key Research Facilities, Infrastructure and Equipment	The Department of Physiology and Pharmacology "Erspamer" has laboratories and facilities for the recording and analysis of preclinical and clinical EEG-EMG-EKG data, analysis of neuroimaging and other biomarkers of neurodegenerative disorders with a focus on Alzheimer's disease and ICT solutions for biomedical applications. The Department of Human Neurosciences has clinical audit, radiology, and biochemical laboratories and facilities for the collection and analysis of clinical, neurological, neuropsychological, diffusion, structural, and functional 1.5 and 3-T MRI, EEG-EMG-EKG, and PET data in patients with cerebrovascular and neurodegenerative diseases with innovative ICT solutions for biomedical applications. The Department of Neurosciences, Mental Health, and Sense Organs has clinical audit, radiology, and biochemical laboratories and facilities for the collection and analysis of clinical, neurological, neuropsychological, diffusion, structural, and functional 1.5 and 3-T MRI, EEG-EMG-EKG, and PET data in patients with cerebrovascular and neurodegenerative diseases with innovative ICT solutions for biomedical applications.
Status of Research Premises	Independent with full unrestricted access to the research facilities necessary to perform the research proposed.

Previous Involvement in Research and Training Programmes,	The research team coordinated by Prof. C. Babiloni has large experience of European scientific projects on neurodegenerative disorders such as **EBRAIN** (HORIZON-INFRA-2021-TECH-01-01; markers for drug discovery in AD, eBRAIN-Health – Actionable Multilevel Health Data), **PharmaCog** (FP7, IMI Joint Undertaking, 2010-2014; markers for drug discovery in AD, www.pharmacog.org), **DECIDE** (FP7, ICT-Infrastructure, 2010-2013; bioinformatics for AD, www.eu-decide.eu), **SRA-NED** (H2020, JPND, 2016-2017; biomarkers of neurodegenerative disorders, www.sra-ned.eu), and **Synanet** (H2020 Twinning, 2016-2018; biomarkers of neurodegenerative disorders, www.synanet2020.com). Prof. C. Babiloni's projects funded by the Italian Ministry of Health are: "Diagnosis of incipient AD development of ADNI-based imaging markers for use by the National Health System" (2009-2011), "Towards Internet-based clinical applications at subjects", "Prediction of cognitive decline in MCI subjects carrying genetic risk factors based on EEG and TMS", and "Does rehabilitation with a 10-Hz sensory stimulation improve brain rhythms and cognitive-motor performance in neurological patients? Towards Internet-based clinical applications at subjects (2011-2014)". GRID-based System for the Evaluation of the Effects of Cognitive Rehabilitation in Patients with Alzheimer's Disease and Parkinson's Disease (2013-2015). Prof. C. Babiloni's project funded by the Italian Ministry of University (MIUR) is "Functional Connectivity and Neuroplasticity in Physiological and Pathological Aging" (2013-2016).
Current Involvement in Research and Training Programmes,	The research team coordinated by Prof. Babiloni is taking part in the project "Peripheral Biomarker Based on Combinatorial Early Diagnostics for Dementia (**CombiDiag**; HORIZON 2021, H2021-MSCA-DN-2021; Grant Agreement: GAP-101071485). It also takes part in the project eBRAIN-Health – Actionable Multilevel Health Data (**eBRAIN-Health**) from HORIZON 2021, HORIZON-INFRA-2021-TECH-01 (HORIZON-INFRA-2021-TECH-01-01 - Interdisciplinary digital twins for modeling and simulating complex phenomena at the service of research infrastructure communities; Grant Agreement: GAP-101058516). The two projects aim to create a scientific multi-disciplinary and multi-national European Consortium and Network-of-excellence implementing an advanced biomedical and biotechnological scientific project in the field of biomarkers and twin brains of AD and other neurodegenerative diseases.
Relevant Publications/datasets/software/ Innovation Products/ other achievements	1. Babiloni C., et al. 2018 *Clin Neurophysiol.*, 129(4):766-782. 2. Babiloni C., et al. 2018 *J. Alzheimers Dis.*, 62(1):247-268. 3. Babiloni C., et al. 2017. *J Alzheimers Dis.*, 59(1):339-358. 4. Babiloni C et al. 2021 *Alzheimers Dement.* 2021;17(9):1528-1553. 5. Babiloni et al. 2020 *Neurobiol Aging*. 2020;85:58-73.

SECTION D. GANTT DIAGRAM



Work Packages (WPs; start and end month, m)
WP1: Coordination, Management, Dissemination, and Communications **1-12 m**.
WP2: Retrospective longitudinal study on multimodal PharmaCog database **1-9 m**.
WP3: Prospective cross-sectional study on multimodal SleepAD database **1-12 m**.
WP4: Translational AI tool models **1-12 m**.

Milestone-Deliverable (M-D, release month, m)
WP1-M-D-1. Annual Report **12 m**
WP1-M-D-2. Project paper and Congress posters; **12 m**
WP2-M-D-1. Project results; **9 m**
WP3-M-D-1. Ethical clearance report; **3 m**
WP3-M-D-2. Project repository at the PDWAVES Consortium platform (www.pdwaves.eu); **6 m**
WP3-M-D-3. Project database and biomarker results; **12 m**
WP4-M-D-1. Validated Artificial Intelligence tools; **6 m**
WP4-M-D-2. Integrated Disease Model; **12 m**

CURRICULUM VITAE OF THE PRINCIPAL INVESTIGATOR

PERSONAL INFORMATION

Full Name: Claudio Babiloni, Born in Rome, 23/03/1962, Italian, **ORCID ID:** 7006669615,
Web: https://web.uniroma1.it/dff/en, www.pdwaves.eu.
Web: https://web.uniroma1.it/dff/it/Laboratorio-di-Neuroscienze-delle-funzioni-superiori-dell-Uomo.

- **EDUCATION**

2001 PhD in Biomedical Sciences, Aalborg University, Denmark;
1997 Master in Clinical Psychology, Sapienza University of Rome, Italy.

- **CURRENT POSITION**

2022 – date Full Professor of Physiology, Dept of Physiology and Pharmacology "V. Erspamer," Sapienza University of Rome, Italy.

- **PREVIOUS POSITIONS**

2012 – 2022 Associate Professor of Physiology, Dept of Physiology and Pharmacology "V. Erspamer," Sapienza University of Rome, Italy;
2007 – 2012 Associate Professor of Physiology, Dept of Biomedical Sciences, University of Foggia, Italy.

- **FELLOWSHIPS AND AWARDS**

2013 Award of Honour - received by the Scientific Committee of the "Second International Conference on Basic and Applied Physiology" held in SMS Medical College, Jaipur, India

2006 Prix Lèon et Henri Fredericq (Classes de Sciences) received by Académie Royale (des sciences, des lettres et des beaux-arts) de Belgique (Degree Diploma)

1996 Prize of Accademia Medica Romana - to develop scientific research with the University of Munich (D).

Oct, 2023. Ranked as Italian "top 39" for ***Neurosciences and Psychology*** by ***Top Italian Scientists***, the World's "top 3" expertise for ***Electroencephalography***, and the World's "top 2" expertise for ***Alpha rhythms*** by ***ExpertScape*** Rating Company.

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS**

2000 – date Scientific mentor of 10 excellent early-stage researchers in Neurophysiology, 12 PhD students, 12 foreign visiting scholars, and several Master students.

- **ORGANISATION OF SCIENTIFIC MEETINGS**

Member of the Organizing Committee of:

- Italian Society of Psychophysiology (SIPF) annual congresses (yrs 2002-2005, 2009, 2002-2023)
- SINdem annual congress (2023)
- 17th European Congress of Clinical Neurophysiology (ECCN; 2019)
- Summer School of the H2020 Twinning Project "Synanet" (June 15th, 2018, Rome, Italy)

Co-organizer and co-chair of:

- "E-PIA Day Scientific Session" the day before the Alzheimer's Association International Conference (AAIC) in 2017 (London), 2018 (Chicago), and 2019 (Los Angeles), 2020 (Virtual), 2021 (Virtual);
- Conference entitled "International Federation of Clinical Neurophysiology Guidelines on the Frequency and Topographical Analysis of Resting State EEG: The Controversies" (September 25th, 2017, Chengdu, China);
- Symposium entitled "Natural History of Dementia with Lewy Bodies: What Prodromal Stage?" (September 13th, 2018, Sapienza University of Rome, Italy);
- "Rome Training Meeting,", as a Member of the Steering Committee of European Horizon2020 Marie Skłodowska Curie project "Blood Biomarker-based Diagnostic Tools for Early-Stage Alzheimer's Disease (BBDiag)," (March 19th -21st, 2018, Sapienza University of Rome, Italy);

- Symposium entitled "Neural Basis of Human Consciousness: phenomena, paradigms, and Exploring Techniques" (June 12th, 2019, Sapienza University of Rome, Italy),
- 5th International Congress of Basic and Clinical Multimodal Imaging (BaCI2021; October 14th-17th, 2021, Virtual)
- 6th International Congress of Basic and Clinical Multimodal Imaging (BaCI2023; September 3rd-7th, 2023, Istanbul)

- **INSTITUTIONAL RESPONSIBILITIES**

2014-2022. Member of the Council of the Doctorate School of Neurophysiology and Experimental-Clinical Neurosciences and Psychiatry, Sapienza University of Rome (Italy).

2008-2012. Member of the Doctorate School of Biomedical Science and Technology Council, University of Foggia (Italy).

- **REVIEWING ACTIVITIES**

2001 – 2023. Ad hoc for International scientific journals: Neurobiology of Aging, International Journal of Psychophysiology, NeuroReport, Journal of Psychophysiology, Psychophysiology, Epilepsia, Cortex, Medical Research Monitor, Brain Research Bulletin, Brain Research, Experimental Brain Research, Journal of Neurophysiology, Journal of Applied Physiology, Brain, Cerebral Cortex, Human Brain Mapping, IEEE Transactions on Neural Systems & Rehabilitation Engineering, IEEE Transactions on Biomedical Engineering. Aging and Clinical Experimental Research. Experimental Brain Research, BMC, PNAS, Journal of Neuroscience, Clinical Neurophysiology, Journal of Alzheimer's Disease, and Current Alzheimer Disease.

2015- 2023. Editorial Board of international scientific journals: Journal of Alzheimer's Disease (Associate Editor 2015 and 2019, Senior Editor, 2012-2014, 2016-2018, 2022), Clinical Neurophysiology (Editorial Board, July 2011-June 2017), NeuroImage (Editorial Board, 2013-2016), Current Alzheimer Disease (Editorial Board, 2016-2023), and Brain Topography (2023).

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

2020-2022 Leader of the Workgroup of the European Chapter of the International Federation of Clinical Neurophysiology (IFCN) to produce the position paper "Recommendations for the Biomarker-Based Diagnosis of Dementia. A European Inter-Societal Delphi Consensus."

2020-2022 Member of the European Chapter of the International Federation of Clinical Neurophysiology (IFCN) Workgroup to produce the Shared European Brain Research Agenda (SEBRA) for H2021-2027 Europe. Partners: (1) Network of European Funding for Neuroscience Research (NEURON); (2) Joint Programme – Neurodegenerative Disease Research (JPND); (3) Human Brain Project (HBP).

2017-2023 Position of "Communications Chair" (2017-2019), "Elected Chair" (2019-2021), "Immediately Past Chair" (2021-2023), and "Advisory Council Officer" (2022-2024) in the Electrophysiology Professional Interest Area (E-PIA) of the "Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) of International Alzheimer Association.

2016 Senior co-leader of the International Federation Clinical Neurophysiology (IFCN) Workgroup "Advanced EEG/MEG Technique in Clinical Neurophysiology."

2002-2023. Italian Society of Psychophysiology (SIPF) Steering Committee as ***Officer*** in 2002-2005 and 2022-2023, ***Auditor*** in 2008-2009

2023-2024. Autonomous Association to Italian Society of Neurology for the Study of Dementia (SINDEM), Scientific Committee as ***Officer*** in 2023-2024

2022-2024. Italian Society of Neurofeedback and qEEG (SINQ), Scientific Committee as ***Officer*** in 2022-2024

2018-2023. Working group of the International Federation of Clinical Neurophysiology (IFCN) for promoting "IFCN Guidelines on EEG" as ***Senior Co-Leader*** http://www.ifcn.info/sigs/sig-functional-brain-connectivity-as-revealed-by-eeg-meg/ from 2018 to date.

2019-2023. Global Brain Consortium Steering Committee as ***Co-leader*** of the Workgroup on "International Clinical Care Translation using EEG" from 2019 to date

Appendix: All current grants and ongoing 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):

Project Title	*Funding source*	*Amount (Euros)*	*Period*	*Role of the PI*	*Relation to current proposal*
Peripheral Biomarker-Based Combinatorial Early Diagnostics for Dementia (CombiDiag)	HORIZON 2021, H2021-MSCA-DN-2021 (Marie Skłodowska-Curie Doctoral Networks) (Proposal number: 101071485)	€ 259,437.60	2023-2027	Principal Investigator of a Research Unit of the University of Rome "La Sapienza" (Italy)	Validation of peripheral biofluid and neurophysiological biomarkers of Alzheimer's disease
eBRAIN-Health – Actionable Multilevel Health Data (eBRAIN-Health)	HORIZON 2021, HORIZON-INFRA-2021-TECH-01 (HORIZON-INFRA-2021-TECH-01-01 - Interdisciplinary digital twins for modeling and simulating complex phenomena at the service of research infrastructure communities) (Grant Agreement: GAP-101058516)	€ 381,245	2022-2026	Principal Investigator of a Research Unit of the University of Rome "La Sapienza" (Italy)	The platform eBRAIN-Health produces Twin Brains as models of the impact of the Alzheimer's disease neuropathology and neurodegeneration on neural circuits and cognitive functions
Effects of endogenous and exogenous risk factors in patients with Alzheimer's and Parkinson's diseases using clinical indexes and endophenotypes (biomarkers) as inputs to artificial intelligence (PREDICT-NEURODEGEN)	Call and Sponsor: ANNUAL STRATEGIC PROGRAM OF ITALIAN MINISTRY OF HEALTH Grant Agreement: PNRR-MAD-2022-12376415	€ 100,000	2023-2025	Principal Investigator of a Research Unit of Sapienza University of Rome (Italy)	Improving the performances of artificial intelligence – machine learning tools in the classification and stratifications of patients with Alzheimer's disease based on disease risk factors and neurophysiological biomarkers of Alzheimer's disease

Assessment of brain functions in Lewy Body disease patients using telemonitoring DIGITAL markers as inputs to artificial intelligence (LBDigital)	ANNUAL STRATEGIC PROGRAM OF THE ITALIAN MINISTRY OF UNIVERSITY AND SCIENTIFIC AND TECHNOLOGICAL RESEARCH (2010SH7H3F) (Grant Agreement: 2010SH7H3F)	€ 75,565	2023-2025	National Coordinator and Principal Investigator of a Research Unit of Sapienza University of Rome (Italy)	Assessment of brain functions in Lewy Body disease patients using telemonitoring digital markers as inputs to artificial intelligence

ALLEGATO C

TABELLA COSTI PERSONALE STANDARD				COSTO DEL PERSONALE
FASCIA DI COSTO /LIVELLO	**NUMERO SOGGETTI**	**COSTO ORARIO vedi nota**	**MONTE ORE**	
Basso	**5**	31 €	425	13.175 €
Medio	**2**	48 €	170	8.160 €
Alto	**3**	73 €	240	17.520 €
TOTALI	**10**		**835**	**38.855 €**

COSTO ORARIO: si deve far riferimento al Decreto Interministeriale n. 116 del 24/1/2018

ALLEGATO C

BUDGET DI PROGETTO	COSTO DEL PERSONALE	OVERHEAD	Costi per servizi di Consulenza Specialistica	Costi per licenze direttamente imputabili al progetto	Costi per materiali e attrezzature direttamente imputabili al progetto	Costi per altre tipologie di spese direttamente imputabili al progetto	COSTO TOTALE
	38.855,00 €	5.828,25 €	0,00 €	0,00 €	10.000,00 €	95.000,00 €	149.683,25 €