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Description of the funded research project

2nd Call for H.F.R.I. Research Projects to Support Post-Doctoral Researchers

MS-NEUROPLAST

Title of the research project
Cognitive decline prognosis in multiple sclerosis: effectiveness of a computerized cognitive training treatment on cortical reorganization

Principal Investigator: Charis Styliadis

Reader-friendly title: Cognitive decline prognosis in multiple sclerosis

Scientific Area: Engineering Sciences & Technology

Institution and Country: Aristotle University Thessaloniki, Greece

Host Institution: Aristotle University Thessaloniki

Collaborating Institution(s): National Neuroscience Institute, Neurophysiology Department, King Fahad Medical City, Riyadh, KSA

Budget: 197.000,00 €

ClinicalTrials.gov Identifier: NCT04806568

Project webpage: http://cstyliadis.webpages.auth.gr/MS-NEUROPLAST.html

Duration: 36 months

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MS-NEUROPLAST Synopsis

MS-NEUROPLAST is a research project of the laboratory of Medical Physics (https://medphys.med.auth.gr/) of Aristotle University of Thessaloniki (AUTH, https://www.auth.gr/en) in cooperation with the Multiple Sclerosis Center (http://ms-center.gr/en/) of the B' Neurological Department of the University General Hospital of Thessaloniki "AHEPA" (https://www.ahepahosp.gr/) and the National Neuroscience Institute, Neurophysiology Department, King Fahad Medical City, Riyadh, KSA (https://www.kfmc.med.sa/EN/Pages/default.aspx).

MS-NEUROPLAST investigates the neuroplastic properties of cognitive training in patients with multiple sclerosis (PwMS), and quantifies through ecologically valid measures of daily activities the MS-related cognitive changes to characterize not only decline but given the right dosage of stimulation improvement as well.

MS-NEUROPLAST challenges

- **Cognitive decline is a debilitating and widespread comorbidity of Multiple Sclerosis (MS) affecting up to 65 percent of PwMS.**
- **Cognitive changes can be the only behavioural index of MS activity. But how accurately and timely can these be captured?**
- **The existing clinical tools are subjective and do not have the dynamic of prognosis.**
- **It remains uncertain how much change in cognitive status is required to translate into a meaningful clinical outcome and how long it may subsequently take to become apparent.**
- **This highlights the need for a parallel to cognitive interventions approach to capture MS-related cognitive impairment via ecologically valid measures.**

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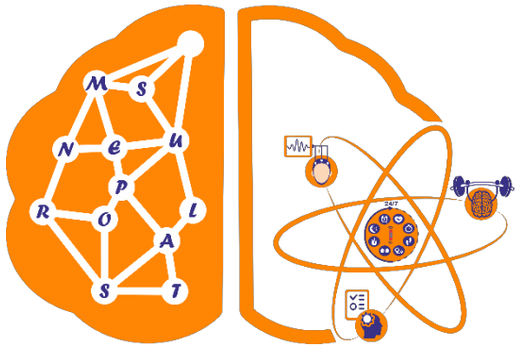
Aims of MS-NEUROPLAST



MS-NEUROPLAST has three main objectives:

- **The in-depth understanding of the neural indices of cognitive impairment in PwMS (i.e., identify decline transition points along the continuum of cognitive capacity).**
- **To dissociate the cortical mechanisms related to training-induced plasticity from those related to maladaptive reorganization due to MS (namely separate good from the bad), by examining whether the correlation of the neurophysiological and cognitive indices with longitudinal ecologically valid measures of daily activities can capture the underlying pathology.**
- **To evaluate the efficacy of a computerized cognitive training treatment for MS-associated cognitive deficits via the dissociation of the cortical mechanisms related to training-induced plasticity from those related to maladaptive reorganization due to MS.**

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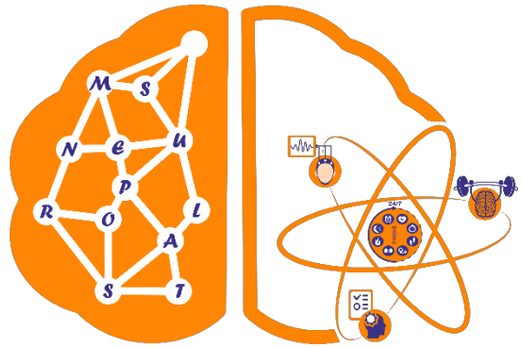
MS-NEUROPLAST Originality



MS-NEUROPLAST includes non-invasive electroencephalography (EEG) recordings, psychometric and somatometric tests, unobtrusive ecologically valid measures of daily activities and cognitive training via the BrainHQ brain-training program. There are no medications or invasive procedures involved.

The course of MS is presumed to be the net result of disease burden and compensatory capacity. The identification of what is beneficial plasticity and by contrast what is maladaptive reorganization in combination with elements of daily functional status can be a game-changer in developing therapeutic strategies able to promote the individual adaptive capacity.

MS-NEUROPLAST goes beyond traditional domains of the care continuum and significantly enhances the clinical domain of PwMS with patient-generated data, such as physical activity data (steps, walking speed), heart rate, oxygen saturation, sleep quality features and other similar variables be seamlessly collected using wearable and ambient devices.

MS-NEUROPLAST's originality is the use of patient generated health data to translate functional health status changes to clinically and neurophysiological meaningful changes related to cognitive status, as well as the protective neuroplastic reorganization of large-scale cortical networks that cognitive training can potentially trigger.

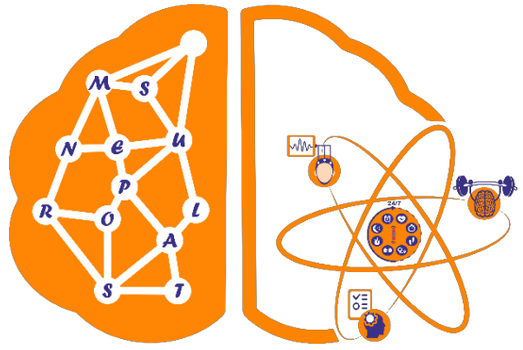
Expected results of MS-NEUROPLAST

Primary outcomes: **Changes in cortical activity strength and cortical connectivity of PwMS in response to cognitive training.**
Change is defined as the statistical significance in the t-test comparison of the current density strength and the cortical connectivity of the reconstructed current density respectively, based on high-density EEG recordings, before and after the training

Secondary outcomes: **Increase in audiovisual integration functionality as measured by the behavioural assessment during the experimental procedure. Change in cognitive functionality. Change of scoring in neuropsychological tests related to attention, memory, and performance, as well as in somatometric tests related to fitness and functional capacity.**
Change is defined as statistical significance in the t-test comparison of the test scores before compared to after the training

Exploratory outcome: **Correlation of the changes of the neurophysiological indices with those of the levels of cognitive capacity and the ecologically valid markers of daily functional status**

Impact of MS-NEUROPLAST



Scientific impact: **The investigation of cognitive network function and dysfunction of PwMs via a cross-sectional and longitudinal approach will allow causality in the inference regarding what is adaptive plasticity in contrast to what is maladaptive reorganization and potentially aid in the reduction of the clinical-radiological paradox. Therefore, a conclusive result regarding the effects of cognitive training will be achieved.**

Clinical impact: **MS-NEUROPLAST's translational approach can reach a concrete conclusion regarding the applicability of cognitive treatment as an intervention for PwMS, and thus lead to improved patient care. The findings may serve not only as recommendations for improving the scientific basis and methodologic rigor for cognitive rehabilitation research but also point towards the development of biologically based theoretical models of cognition capable of empirical validation and evidence-based refinement, providing the scientific context for effective personalized treatment discovery.**

Economic and societal impact: **MS has a determinant effect on the social, working, and daily life of patients. Also, it places significant strain on the patient's caregiver. These facts raise serious concerns regarding the quality of life of PwMs and the financial sustainability of healthcare systems. The translation of MS-NEUROPLAST's achieved neuroscientific knowledge can inform on the benefit of timely implementation of the right intervention allowing for enhanced quality of life outcomes for as long as possible. The intervention is based on BrainHQ and thus can be performed via smart devices by the majority of PwMS. Ensuring the easy and widespread applicability of the intervention with a minimum cost on human resources promotes the financial sustainability of healthcare systems. The remote approach of the intervention opens up participation for individuals who are largely home-based or who or struggling to maintain employment and reluctant to participate in rehabilitative activities that would interfere with their work and family time commitments.**

The importance of funding MS-NEUROPLAST

MS-NEUROPLAST can provide a significant building block on the PI's career. This project will strengthen and expand the PI's scientific cooperation with the with the Multiple Sclerosis Center of the University General Hospital of Thessaloniki "AHEPA" and the National Neuroscience Institute of King Fahad Medical City.

MS-NEUROPLAST results will be initially disseminated as research articles in peer-reviewed journals, book chapters, and conference proceedings in the field of cognitive and clinical neuroscience and neurology. Also, the results of the project will be disseminated through courses, lectures and teaching at the Aristotle University of Thessaloniki.

The expected outcomes on understanding cognitive deficits in MS, the neuroimaging of neural bases and correlates of deficits, and the development of effective treatments will be further exploited by the PI by setting up new collaborations and authoring new research proposals targeting similarly critical challenges in the field of neurodegeneration.

Within this plan, other research teams, and relevant institutions and authorities will be involved to establish a multidisciplinary research group that will evolve the PI's research activities and expertise.

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