alessandro.villa@unil.ch   alessandra.lintas@unil.ch

Enhancing Cognitive Resilience (ENCORE)

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterised by widespread pathological changes in the brain, including the accumulation of amyloid-beta plaques and neurofibrillary tangles of tau protein, leading to symptoms like memory loss, personality shifts, and impaired judgment. Similarly, in Mild Cognitive Impairment (MCI), a condition sharing similar symptoms with AD but in milder forms and occasionally progressing to full-blown AD, individuals are characterised by cortical alterations in neural dynamics and some level of amyloid-beta and tau, albeit to a lesser extent than in AD. The risk of cognitive decline significantly increases with age, and women, who tend to outlive men, are more likely to reach this vulnerable stage of life. In the United States, about two-thirds of AD patients are women, as reported by the Alzheimer's Association.

Previous research using functional Magnetic Resonance Imaging (fMRI), electroencephalography (EEG), or magnetoencephalography (MEG) has revealed that during working memory (WM) tasks, specific patterns of neural activity and connectivity emerge within cortical circuits, involving activation of prefrontal and parietal areas. Working memory training (WMT) has been the subject of research and interest in the field of cognitive science, particularly with regard to its potential benefits for individuals with AD/MCI. Some studies have shown promising results on the effectiveness of WMT, particularly in individuals with MCI and early-stage AD, showing benefits that could extend to other domains of cognition and daily functioning. Given these considerations, this research project focuses on female AD/MCI patients classified according to their clinical screening with two primary objectives.

Our first objective is to investigate changes in fast brain activity among individuals with AD and MCI in comparison to healthy individuals. Participants will undergo tests assessing their attention and working memory functions, employing the Attention Network Test and the Dual n-Back memory task. We will monitor their brain activity both during rest and while performing these cognitive tasks using non-invasive EEG and frequency-domain functional near-infrared spectroscopy (FD-fNIRS) to capture fast optical signals. Various spatial, temporal, and correlational features of brain signals will be analysed to identify potential biomarkers useful to determining their association with test results and diagnostic categories (MCI, AD, or control). The second objective focuses on assessing whether active engagement in WMT with the Dual n-Back memory task can enhance behavioural performance, and if so, identifying physiological markers that consistently correlate with this improvement. Following one month of daily at-home WMT, participants will return to the laboratory for a post-training evaluation of their performance, as well as for a second round of EEG and FD-fNIRS recordings during rest and task execution. These post-training assessments will be followed up at the 3-month, 6-month and 12-month sessions. The secondary goal is to establish whether the physiological changes that co-occur with improved performance, if detected, align with the brain-activity markers identified in the first objective as reliable predictors of cognitive reserve and diagnosis.

This research project will yield two major scientific outcomes: Firstly, the simultaneous EEG and FD-fNIRS recordings will provide a deeper understanding of cortical activity in individuals with AD/MCI and may reveal potential biomarkers for diagnosing these conditions. Secondly, our project's core objective is to enhance the quality of life for patients. If our WMT approach proves successful, it will offer valuable insights for designing behavioural therapies for individuals with AD/MCI. This is a collaborative project carried out by Swiss and Argentinian teams lead by women with their complementary specific expertise. At the end of the project, several aspects will have an impact on society, beyond the advancement of science. This project underscores the importance of women's roles in science, both in the context of our specific focus on AD/MCI in women and in the leadership roles held by the researchers leading these investigations. In addition, the project's innovative approach holds the potential to foster growth through innovation, leading to the creation of additional high-quality jobs in the field of cognitive remediation. This becomes especially relevant in the absence of a viable pharmacological solution to mitigate the progression of Alzheimer's pathology.