

1. Summary for publication: 2nd project period (01.10.2019 – 31.03.2021)

1.1 Summary of the context and overall objectives of the project

Stress-related disorders such as anxiety, depression or post-traumatic stress disorder pose a significant burden on individuals, the economy, and society in general. The prevalence of these disorders has not decreased in the past decades, despite huge efforts that have been made in research on disease mechanisms and treatments. More recently, evidence has accumulated for an exacerbation of stress-related public health problems, in particular in young people. The COVID-19 pandemic has further highlighted the societal relevance of stress-related burden. The overall aim of DynaMORE (Dynamic MOdelling of RESilience) is to improve the prevention of, or quick recovery from, stress-related mental health problems. DynaMORE's approach is health- rather than disease-focussed, that is, we try to avoid mental problems rather than trying to cure them after they have already developed into full-blown psychiatric diseases. Eventually, this will increase individual well-being and reduce healthcare demands and indirect economic costs.

DynaMORE pursues this goal by advancing the mathematical modelling of mental health, helping us also to deepen our scientific understanding; by generating and validating the first in-silico model of stress resilience; and by using it as a basis for developing an entirely new mobile Health (mHealth) product for the primary prevention of stress disorders, with great potential for commercial exploitation. We anticipate that our solutions will be pandemic-proof and facilitate coping with future pandemics for individuals and for societies at large.

1.2 Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

DynaMORE work packages (WPs) 1 to 3 developed a basic theoretical approach to the mathematical modelling of resilience and techniques to analyse real-world data from longitudinal resilience studies in individuals exposed to stressful life situations. These techniques include improved ways of quantifying resilience – understood as the maintenance or quick recovery of mental health during and after stressful life periods (Kalisch et al., psyarxiv.com/jg238/, 2020) – and of predicting such good mental health outcomes (Köber et al., www.medrxiv.org/content/10.1101/2020.08.18.20177113v1, 2020). DynaMORE WP 3 has applied these techniques to existing data sets, while WP 4 has conducted several studies during the COVID-19 pandemic (e.g., Veer et al., *Translational Psychiatry*, 2021) in which these techniques are used. First results point towards a key role for positive appraisal style, originally posited in 2015 by DynaMORE researchers as a major resilience mechanism (Kalisch et al., *Behavioral and Brain Science* 2015). To further test this and other identified resilience factors and to establish a formal mathematical model, WP 4 is currently conducting a longitudinal multi-center study at sites in Germany (Mainz, Berlin), the Netherlands (Nijmegen), Poland (Warsaw), and Israel (Tel Aviv). The study is using extensive baseline subject characterization, including with a neuroimaging battery specifically adapted for this project from experiences in an earlier study (Kampa et al., www.biorxiv.org/content/10.1101/470435v1, 2018; Kampa et al., *Neuroimage*, 2020), high-frequent online mental health, stressor and resilience factor monitoring (Kalisch et al., psyarxiv.com/jg238/, 2020), as well as ambulatory methods, using ecological momentary assessment of stressors, emotional states, and physiological reactions, as developed by WPs 5 and 6. Currently, DynaMORE is working towards exploiting the knowledge gained through these studies in developing smartphone-app based ecological momentary interventions (EMIs) that are designed to boost specific resilience factors and will be used in a second multi-center study as a means to improve resilience. This will allow for testing the causal role of the targeted resilience factors, for finding out who benefits most from them, and for refining the resilience model. Moreover, the study will be a prototype test of a new mHealth application that combines individual characterization, mathematical modelling and longitudinal assessment data.

DynaMORE is also a project that is dedicated to the training and mentoring of its junior staff, for who a program with a retreat, a workshop and two international symposia as well as a mentoring structure were designed by WPs 8 and 9. WP 8 developed an open-science policy. WP 9 made important efforts in the dissemination and communication both to the scientific community and to the lay public.

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1.3 Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

DynaMORE will develop resilience research into a discipline that increasingly uses the methods of exact mathematical science to predict results, test interventions and generate new manipulations intended to support the prevention of stress disorders. This goal is intertwined with the objectives to gain a better understanding of resilience and, moreover, to find new ways to combat stress-related disorders. If successful, our approach will help improve public health and reduce the individual, societal and economic burden of stress-related disorders. DynaMORE will also advance the field of in-silico modelling and simulation, through the refinement of existing and the generation of new methods, and promote health technology, through the development of a product prototype with significant potential for commercial exploitation and valorisation. We further expect wider impacts on the fields of computational psychiatry, in particular in the areas of disease prediction and prevention.

1.4 Address (URL) of the action's public website

<https://dynamore-project.eu/>