1. Summary for publication: 1st project period (1.4.2018 – 30.9.2019)

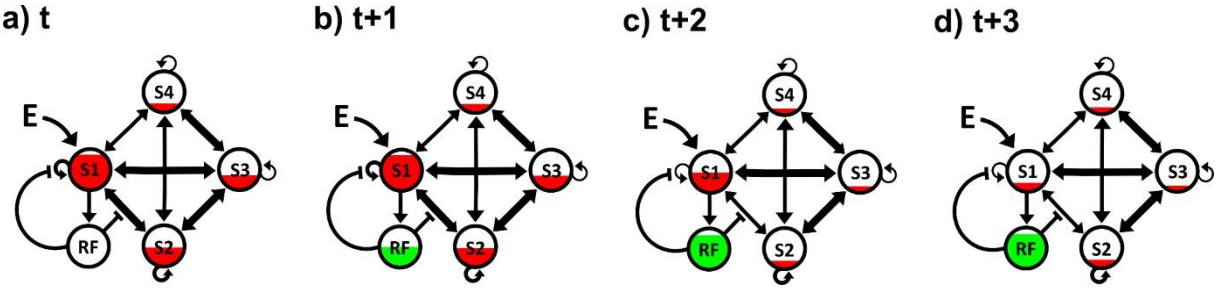
1.1 Summary of the context and overall objectives of the project

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 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.

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 that is based on the conceptualization of stress-related disorders as dynamic networks of interacting symptoms that may be driven by stressors into stable states of disease. Resilience factors are incorporated into these networks as new network nodes, which are able to dampen symptom interactions and prevent the system from transiting into a disease state. Resilience factors themselves can vary over time in their strength (effectiveness). The basic idea is illustrated in Figure 7 of our common publication (Kalisch*, Cramer* et al., Persp. Psychol. Sci. 2019). In the figure, S1 to S4 are stress-related symptoms, E is a stressor and RF is a resilience factor. The symptom is the higher, the higher the red filling of the node. Symptom activation spreads across the network from S1 to other symptoms via the symptom interconnections (arrows). Activation spread is limited by the inhibitory connections from the RF to the interconnections. The strength of the RF is indicated by the green filling of the node. Use of an RF may be motivated or strengthened by an aversive emotional state (stress; arrow from S1 to RF). t, time point.



Mixed autoregressive models are used to model such networks, based on empirical data from two on-going longitudinal resilience studies, MARP (Mainz Resilience Project) and LORA (Longitudinal Resilience Assessment). Methods to quantify resilience based on regular online monitorings of mental health and stressor exposure (adversity), to deal with missing data, and to identify resilience factors from the MARP and LORA projects have also been developed by the WPs. On this basis, WP 4 has designed a first longitudinal multi-center study, to be conducted in Germany (Mainz, Berlin), the Netherlands (Nijmegen), Poland (Warsaw) and Israel (Tel Aviv) that will test the model. The study will use extensive baseline subject characterization, including with a neuroimaging battery specifically adapted for this project from experiences with MARP, and high-frequent only mental health and stressor monitoring, also refined based on prior experience by WP 4. The subject monitoring methods in this study will further be extended to ambulatory methods, using ecological momentary assessment

of stressors, emotional states, and physiological reactions, for which WPs 5 and 6 have developed dedicated methods. This will allow even better modelling. WPs 5 and 7 have developed a first smartphone app-based intervention that is intended to boost an identified resilience factor, is now being tested for its effectiveness, and will then be used in a second multi-center study as a means to causally intervene into the network. This will allow for testing the causal role of the identified factor. Moreover, the study will be a prototype test of a new mHealth application that combines individual characterization, mathematical modelling of baseline and longitudinal assessment data, and – on this basis - personalised, targeted intervention with the aim to prevent stress-related pathology.

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.

1.3 Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the action 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/