Health & Technology
By Convergence

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Integrative Neuromedicine (IN)

Leads

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Summary

Over 250 million people suffer from Neurological Disorders (NDs) globally, of which approximately 41 million live in Europe. Treating NDs accounts for 35% of Europe's total disease burden with a yearly cost of €798 billion. Yet comprehensive treatments for NDs are lacking.

NDs are complex at many levels: from molecular mechanisms through cellular manifestations and brain-wide effects, to the experience by individual patients and societal interpretation and acceptance. Current large-scale efforts to understand or treat NDs therefore rarely meet with complete success or universal acclaim. In this flagship, we propose to lay the groundwork for an integrative multidisciplinary approach that is necessary to understand the intricacies of ND manifestation, from the cellular to the phenomenological level. We will investigate NDs across scales, from molecule to society; across time, from conception to death; and across approaches, from biological to philosophical.

This flagship aims to create the first-of-its-kind cohesive and synergistic pipeline for the investigation and treatment of NDs. Through this pipeline we will accelerate the translation from therapeutic ideas to the clinical stage in the next 5 to 10 years. Concretely we will focus on the mTOR pathway, which is central to many NDs, including autism spectrum disorders and epilepsy.
The project consists of three Work Packages: **Mapping**, which focuses on techniques to acquire fundamental information about the brain throughout life; **Understanding**, which seeks to inquire, at every level, the difference between normal and diseased brains; and **Intervention**, which aims to translate findings to effective and accepted diagnostics and treatments. The project will fundamentally change the way NDs are being researched and treated. We will increase efficacy and usefulness of fundamental insights; increase the speed of bench to bedside translation; and increase the success and acceptance of proposed interventions, with the final aim of significantly decreasing the impacts of NDs

2022012

Proactive Technology-supported prevention and Mental Health in adolescence (Protect ME)

Leads

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Summary

Societal problem. 13-25% of Dutch youth (aged 12-25) suffers from depression or anxiety. Such mental health problems have long-lasting negative effects, including educational dropout, worse physical health, and increased inequality. Mental health problems cost Dutch society 2 billion euro annually. Adequate and timely identification and treatment are currently impossible, due to long waiting lists, time-consuming monitoring procedures, and the lack of personalized, proactive prevention strategies. Hence, systematic changes in our approach to youth mental health are sorely needed.

Scientific ambition:
Optimizing the well-being of Dutch youth aged 12 to 25 by: (WP 1) improving early identification of mental health problems, using cutting edge real-time measures, smartphone and wearable technology, and data modeling; (WP 2) improving decision making of who needs which intervention and when, combining professional expertise with artificial intelligence; (WP 3) creating and evaluating new technology-driven proactive interventions (e.g., eHealth). Our integrated approach involves stakeholders and end users in each step (WP 4); and builds a sustainable infrastructure and collaboration for convergence and impact (WP 5). Output, outcome, impact. Apart from obtaining ground-breaking scientific insights into the antecedents of mental health problems, we will immediately provide new ways to improve detection, decision making and intervention, new methods and approaches, and user-friendly and cost-effective solutions for youth and professionals. In the long-term, this results in proactive, personalized, accessible, and cost-effective prevention of mental health problems, based on a sustainable business proposition.

The ultimate impact will be a decrease in adolescents entering specialized mental health care, shorter waiting lists, a significant reduction in societal costs of adolescent mental health problems, and, most importantly, the optimal well-being of all youth. Fit to convergence. Medical sciences, social science, humanities, and technology converge to promote this grand transition in mental health care, for those who need us most: Our children, our future.

2022017

Convergence Imaging Facility and Innovation Centre (CIFIC)

Leads

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Summary

We aim to create a convergent imaging facility and innovation center (CIFIC) that accelerates the pace of innovation and application in bio-imaging and microscopy. CIFIC brings an integral approach, where innovation in microscopy is delivered by a flagship facility that provides both beyond-state-of-the-art equipment and an expertise and innovation ecosystem. This unique combination of technical and theoretical expertise (TU Delft), biomedical expertise (Erasmus MC) and innovation management and initiative (EUR) has several key advantages and opportunities:

1. It creates an extensive mutual feedback-loop between technology development and application at the various Technology Readiness Levels.
2. It enables optimization of an entire workflow, from sample preparation protocols such as tissue preservation and clearing, molecular probes and contrast agents, a set of interconnected instrumentation hardware, to computational algorithms and data analysis techniques tailored to specific biomedical applications.
3. It stimulates commercialization and market readiness by continuous feedback along the entire innovation and Technology Readiness Level (TRL) chain. The proposed way of working is also an attractive value proposition for industrial partners to set up collaborations and cultivate entrepreneurial activities originating from the work.

Interactions between the TU Delft and Erasmus MC groups (mutual feedback loops) will be catalyzed by the Optical Imaging Centre (OIC), a core facility (CoFa) at Erasmus MC, with an excellent reputation for translating fundamental, translational and (pre)clinical research questions into specific microscopy applications. This catalyzing role will be strongly enhanced by close collaboration with the Van Leeuwenhoek Laboratory for Advanced Imaging Research (VLLAIR) at TU Delft, which hosts a range of microscopy pioneers targeting fundamental technology breakthroughs and instrumentation innovation co-developed with industrial partners. Innovation and commercialization will be further accelerated via support from the Erasmus Center for Innovation, whose members are specialized in collaboration creativity and learning management in large multiparty innovation networks.

2022020

Healthy Joints

Leads

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Summary

Healthy Joints are essential for physical functioning throughout life. Among joint diseases osteoarthritis (OA) has the highest prevalence and disability. In coming decades OA will become the most common chronic disease in the Netherlands. There are still enormous challenges in OA, ranging from poor understanding about the disease to insufficient early diagnostics and ineffective and non-personalized treatment strategies. To move the field forward, we aim to prevent, diagnose and treat OA at an earlier stage, and target personalized management. For this, it is imperative to improve our understanding of OA phenotypes and how these can be detected early, to develop and apply innovative technology at all anatomical scales and phases of the disease, and to develop and test preventive or early-stage personalized interventions. These efforts will be aligned with the stakeholders' acceptance, and behavioural aspects.

The flagships' researchers with fundamental biological, social, medical and engineering backgrounds will join forces to address:
1) Developing precise personalized computational models for healthy joint growth and maintenance, assess joint load in high-risk and early-stage OA groups, enabling artificial testing of new and precise preventive and early-stage interventions;
2) Build cellular models for different joint tissues and phenotypes to identify personal drivers of OA, and use joint-on-a-chip to test interventions at cell level;
3) Improved and novel diagnostics based on novel hybrid imaging modalities and computational biomechanics enabling the early diagnosis of adverse cartilage load and metabolic joint processes and subsequent targeted therapy;
4) Machine-learning techniques to better recognize the early imaging joint tissue changes, and the phenotype specific patterns;
5) Test preventive treatment, early-stage diagnostics and treatment combined with behavioural insights and stakeholder choices. The long-term goal of Healthy Joints is to prevent OA where possible, or identify the disease early and precise, to allow early-personalized treatment, yielding at least 5 good quality-of-life years.

2022025

Organ Transplantation: making unsuitable donor organs suitable

Leads

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Summary

Ageing and lifestyle changes lead to population alterations and are increasingly affecting social and health related issues. These changes do have an impact on organ transplantation where patients of all ages need highquality organs to be transplanted successfully. Organs retrieved from elderly, obese or unhealthy lifestyle donors and those donated after cardiac arrest do not recover from injury inherent to surgery as completely as young organs. Therefore, there is great reluctance to accept organs of marginal donors because of fear of nonfunction in the recipient. At present, the availability of donor organs is desperately insufficient to meet the need, and new strategies are needed to solve the donor organ shortage.

For some, living organ donation may be a successful alternative but finding a relative to donate might not always be an option as for lung and heart donation. Most patients will remain dependent on deceased organ donation, facing a 20% mortality rate on the transplant waiting list. Alternative options like dialysis, and pulmonary or cardiac support may be offered albeit with increased risk on morbidity and early death. Obviously, the current situation necessitates the development of new strategies.

In this Flagship, we envision technological innovation to build a longterm machine perfusion platform to not only sustain but also recover donor organ viability outofthebody. Damaged donor organs will be made suitable for transplantation. The Erasmus MC is needed to deliver fundamental insights in cellular and tissue repair, targets for pharmacotherapy and stem cell knowledge for regenerative medicine approaches to preserve, repair and regenerate organs for transplantation.

A breakthrough technological innovation from TU Delft is needed to integrate machine components, optimize regulatory feedback systems, and miniaturize the system, while EUR expertise is needed to compare the outcome of these developments with alternatives in terms of costs, (heathrelated) benefits, patient/societal preferences, and ethical aspects.

2022026

Consultation Room 2030 - Continuity of care from hospital to home

Leads

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Summary

Sustainability of healthcare is under pressure because of staff shortages, financial limitations, and societal expectations. Technological innovations could offer solutions, but many innovations in healthcare are characterized by non-adoption or by failed attempts to scale up, spread distantly, or sustain the innovation long term at the organization or system level. Embracing the possibilities of digital health technologies requires rethinking of the processes in the traditional consultation room.

This Flagship takes up the challenge of designing the Consultation Room of the future inand outside the hospital through building on existing initiatives (level 1), connecting, comparing, and integrating what is required for these initiatives to become embedded sustainably in the broader healthcare system (level 2) and by extending our network while facilitating learning and identifying the most promising solutions (level 3). Within this Flagship 7 PhDs, a Post-Doc and researchers from Erasmus Medical Center, Erasmus University Rotterdam and TU Delft contribute to the aim to shape the (conditions for the) continuity of care from hospital to home through digital technologies, in which:
1) digital technologies for various conditions are integrated via codesign in care pathways;
2) the embedding of these technologies is addressed from an interdisciplinary perspective;
3) the impact of the digital technologies is continuously monitored through formative evaluation developed for different types of outcome measures and soft impacts.

One of the goals is to become a Centre of Expertise on digital health by identifying the most promising approaches to structurally embed such technologies in care networks and facilitate inter-organizational learning. This will facilitate a sustainable, interdisciplinary research group with the ability to provide solutions for current healthcare issues and to proactively facilitate future changes in healthcare.

2022030

A Lifecourse and Individual-based View on Lifestyle to Enhance Health (ALIVE)

Leads

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Summary

Lifestyle factors such as physical activity, diet and sleep are crucial for an individual's health throughout life. To ensure lifestyle interventions are more successful at improving health, an individual-based approach should be adopted, taking into account an individual's diverse and changing characteristics, such as life stage and socio-economic status, and their attributes such as personal goals and preferences. The overall objective of ALIVE is to contribute to the development of more effective, individualbased lifestyle interventions by establishing a research infrastructure, by focusing on individual characteristics and attributes across the lifecourse, and by developing strategies to improve existing interventions in order to maintain and/or acquire health.

As combined knowledge, technologies and resources across academic disciplines are needed to achieve this objective, ALIVE is a collaboration of TU Delft, Erasmus MC and Erasmus University. Although our long-term aim is to provide the tools to improve any type of health, we will focus on brain and mental health within the first 5 years, creating transferable knowledge, skills and a research infrastructure.

Our aims are to:
1. Create a data science network to collect, combine and provide data to support crossstudy (e.g., cohorts, registries, national databases) and multidisciplinary research collaborations.
2. Develop new and improve existing quantification methods for lifestyle behaviors across individuals using state-of-the-art device-employed measures to more precisely estimate associations with health.
3. Unravel the multidimensional interactions between lifestyle and their effects on maintaining and acquiring health across individuals over the lifecourse.
4. Design tools to identify individual attributes, such as personal goals and preferences regarding optimal health and lifestyle, as well as tools to address those attributes in health interventions.
5. (Re-)evaluate existing interventions and policies using a novel individual-based approach and new (combinations of) data to develop recommendations, guidelines for practitioners, and applications across health care and policy.

2022031

Personalized, Real-Time Health Impact of Climate Change and Pollution

Leads

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Summary

Prolonged exposure to excessive heat and environmental pollution is associated with increased risk of chronic diseases including cancer, cardiovascular, and neurological diseases. The current course of global climate change and decreased environmental quality puts 3.5 billion people in danger, disproportionally affecting disadvantaged populations and increasing health inequalities. To significantly improve population health, targeted and timely interventions are key. Current research linking environmental stressors and health is, however, limited to long-after-the-fact large-scale statistics and longterm trends, restricting our ability to adapt behavior & provide cost-effective, timely, personalized prevention and treatment strategies. In our Flagship, we propose a radically different approach (Scheme below).

We advance and combine key developments in bioengineering, medical wearables and data-driven impact analysis – supported by clinical, economic and ethical insights – to unveil and mitigate the effects of environmental stress on an individual scale in real time from the tissue to the societal level:
1. Biological response at the tissue level: develop organ-on-chip platforms for in-depth investigations of the personalized biological response towards environmental stress.
2. Real-time response at the individual level: develop wearable skin patches for a) personalized, real-time biomarker sensing and b) monitoring and understanding individual behavioral response towards environmental exposure.
3. Behavioral and health response at the individual and societal level: combine personalized wearable sensors with advanced data analytics to develop individualized interventions and cost-effective policies.

These breakthroughs will enable evidence-based personalized interventions, providing citizens and clinicians with the toolsets and knowledge to implement personalized prevention and treatment strategies, while empowering policy-making agencies with analytics based on real-time data to develop cost-effective and ethical policies for mitigating environmental health challenges.

2022035

Convergence in a dish: Individualized CELLular models of disease diversity in the population

Leads

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Summary

Every person is unique and therefore we observe large differences between individuals in disease risk, treatment response and other human phenotypes.This diversity originates from an interplay between geneticand environmentalvariations. Optimal disease treatment or prevention for each individual requires a better understanding ofthe complex biology behind this interplay. Human disease modelling has been revolutionized by the arrival of inducedpluripotent stem cells (iPSCs), which enables the generation of cellularand tissuemodelsfor each individual. Most iPSC studies have been conducted on a small number of donors(<10), but recent technical developmentsprovide unique opportunities for large-scale applications(hundreds to thousands).

OurFlagship "Convergence in a dish" proposes to build a novel platform to develop, test and apply large-scale Individualized CELLular models (iCELL) across the normal population, to capture and understand (genetic) diversity between individualsin complex diseases, such as neurodegenerative disease, osteoarthritis and cancer.We will use"village cultures", where iPSCs from many individuals are co-cultured using homogeneous conditions across the village. This cost-effective design will be coupled to innovative cellular/ molecular phenotyping:high-throughput spatio-temporal imaging in combination with image-guided optogenetic selection of single cells harboring specific phenotypes followed by single cell RNA/DNA sequencing and proteomics. We will further improve the iCELL models by mimicking the naturalenvironment of cellsand tissues, as well as including intrinsic (e.g.,genetic)and extrinsic (e.g.,environmental) factors relevant forthe diseases interest. Although iCELL can be used to study all diseases, wewill focus ontwo examples: DNA-repair and fibrosis.

We will create computational models based on game theory and machine learning to analyze individual disease characteristics and predict their response to treatment. In addition, applications of iCELL technology will be guided in an interactive co-creation process, where ethics, cost-benefit and public awareness will be evaluated together with valorisation opportunities.

2022036

Convergence Human Mobility Center

Leads

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Summary

Demand for healthcare is growing and becoming increasingly complex. Stroke is in the top five of diseases with the highest annual care costs, where patients face numerous obstacles in accessing the necessary care for rehabilitation. Moreover, as society ages, the number of stroke patients is expected to increase. A paradigm shift is needed from conventional on-site labour-intensive motor rehabilitation to minimally supervised motor rehabilitation at the patient's home. Initiated by partners from TU Delft, Erasmus MC, EUR, Rijndam Rehabilitation and Laurens geriatric rehabilitation, the Convergence Human Mobility Center (CHMC) will enhance the effectiveness and acceptability of user-centred technology-based minimally supervised motor rehabilitation interventions in stroke with equal access for all. This requires integrating expertise in motor learning, sensors and robotics, data science and AI, and biomechanical modelling. In addition, it also requires understanding the complexity of settings and attitudes and beliefs of both clinicians and patients, including vulnerable patients and patients with a low socioeconomic status (SES).

To reach beyond the initial implementation phase we will integrate four main pillars:

- 1. identifying requirements of user-centred minimally supervised treatment that also targetlower SES and vulnerable patients,
- 2. optimizing the effectiveness of (remote) motor learning programmes by exploiting the relation between motor learning, motor capabilities and daily life performance and behaviours,
- 3. engineering home training environments that leverage novel ultra-low-cost technological solutions that are minimalistic and easy to use to promote the transfer of trained skills to activities of daily living,
- 4. developing unobtrusive remote monitoring and feedback based on sensor fusion and modelling to quantify patient performance in their natural environment and to ensure their safety.

The future impact goes beyond the stroke population and will include other neurological and musculoskeletal diseases, like multiple sclerosis, spinal cord injury, Parkinson's disease and osteoarthritis, which limit mobility.