Neuroscience Letters 749 (2021) 135790

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Introduction: An overview of NIMH (Klecany, CZ) scientific activities

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ARTICLE INFO

Keywords:
Applied neuroscience
Biological psychiatry
Social psychiatry
Neuropsychiatric research
Mental health care

ABSTRACT

An overview of research activities of National Institute of Mental Health (NIMH) in Klecany, Czech republic. The institute was funded by EU operational project Research and Development for Innovation and started working in 2015. NIMH activities are organized in eight research programs including the neurobiology of the serious mental disorders, social psychiatry, brain imaging and use of information technologies in psychiatric research, epidemiology of addictions, sleep laboratory and chronobiology, electrophysiology, clinical research, and transfer of technologies. The equipment and expertise ranks NIMH Klecany among top neuroscience research institutions in central and eastern Europe.

National Institute of Mental Health (NIMH) in Klecany, Czech Republic (Photo 1), funded between 2011–2015 by EU operational project Research and Development for Innovation, became soon a prominent research and training center for the field of mental health in Central and Eastern Europe. The NIMH research is focused particularly on the neurobiology and translational research of severe mental disorders, such as schizophrenia, bipolar disorder, and anxiety, sleep, and cognitive disorders. Among the R&D goals of NIMH is also the development and testing of new diagnostic and therapeutic methods and tools. To address the issue, combinations of methods of molecular biology, animal models, and clinical research and testing are implemented. Importantly, NIMH also covers crucial activities in public mental health and social psychiatry, participating significantly in governmental mental health care reform. (2019 Annual report see at hoschl.cz/ATVF).

NIMH amalgamates eight large research programs (1-8), with each comprised of several working groups addressing specific translational and research topics. (1) the neurobiology of the serious neurodegenerative and psychiatric disorders and addictions, (2) the reform of mental health care and development, and testing new services and interventions, (3) building a multimodal database for advanced data analyses and monitoring brain states, (4) the epidemiology of non-transmissible diseases including addictions, and on evaluating the effectiveness of mental health care system to reduce socioeconomic burden of mental disorders, (5) research and innovations of the treatment of sleep disorders and circadian rhythm impairments, (6) electrophysiological, (7) clinical, and (8) translational neuroscience research.

The research program (1) (RP1) has been developing primarily the following thematic priorities: Neurodegenerative diseases - elucidating the mechanisms and pathobiology of 17ß-HSD10 interactions with cyclophilin D in Alzheimer's disease and related dementias; advancement and validation of autoantibody-based diagnostic assays for early detection and differential diagnosis of Alzheimer's and Parkinson's diseases, Frontotemporal Dementia and related conditions; investigating the role of BDNF signaling in driving the differentiation and polarization of developing neurons, via post-translational modifications of the microtubule-associated protein tau in neurons and neuron-like cell lines. Behavioral studies with analysis of structural and functional plasticity in the tsc2 loss-of-function rat model of autism and many other topics are also on the research agenda of the program. Recent publications of the RP1 group present analysis of BDNF signaling and neuroplasticity [1], the neurobiology of Alzheimer's dementia [2], the molecular basis of the SARS-CoV-2 Coronavirus [3], and neurobehavioral correlates of methamphetamine and sleep [4].

The overarching aims of the RP2 is to generate evidence for informed decision-making in the field of mental health care and to trigger improvements in this field through the development and piloting of new clinical psychiatric services and interventions. The most important results of this program have been presented in recent papers focused on the prevalence of mental disorders and disability [5], the development of mental health care for people with severe mental illnesses in central and eastern Europe [6], and on the impact of Covid-19 disease on mental health [7].

The primary targets of RP3 (Applied Neurosciences and Brain Imaging) have been recently defined and addressed by the collaborative initiatives established between NIMH and some of the country's largest

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https://doi.org/10.1016/j.neulet.2021.135790
Received 26 January 2021; Accepted 24 February 2021
Available online 27 February 2021

Photo 1. NIMH Klecany, Czech Republic.

psychiatric hospitals. The NIMH consortium comprised a total of 22 psychiatric inpatient facilities, which enabled to build the world's largest multimodal database of patients with the first episode of schizophrenia (FES). RP3 is currently monitoring 370 patients with FES and 280 healthy controls. Each visit includes an MRI, blood sampling with detection of ~40 markers, a comprehensive neurocognitive examination, EEG, anthropometry etc. The database currently contains in total of 1,119 such complex examinations and is open for sharing for research. The team has recently identified latent classes of FES spectrum patients based on distinct patterns of progressive brain cortical reorganization as assessed by longitudinal surface-based functional measurements. These findings were have been validated employing voxel-based and deformation-based morphometric approaches. The emerging evidence suggests a wide range of subtle and clinically relevant features of brain cortical reorganization in schizophrenia, representing different putative neurobiological subgroups. The subtyping model approach is now subject to the UK patent pending (UK patent GB2000634.2). Our recent publications also cover the seasonality of major mental disorders [8], morphological changes related to psychopathology [9,10], and staging of schizophrenia using psychometric scoring [11].

The main priority of RP4 (Epidemiological and Clinical Research in Addictions) is to provide innovative and effective epidemiological information on substance use in the Czech Republic, to evaluate the effectiveness of the prevention and treatment schemes and systems, to reduce the negative impact of substance abuse on health and well being, and to define its economic and social consequences. The team reported recently changing trends in alcohol use among Czech school-aged children from 1994 to 2014 [12], cannabis availability among Czech urban youth [13], and assess the use of alcohol and its consequences [14].

The Sleep Medicine and Chronobiology program (RP5) works to improve the diagnostics and treatment of patients with sleep disorders and advances the research of disruptions of circadian rhythmicity with an emphasis on early-stage detection, long-term monitoring, and preventive potential of early functional and pharmacological interventions. Main recent publications from this program cover methodology of polysomnography [15], circadian rhythmicity [16], and REM sleep behavior disorder [17].

RP6 (Brain Electrophysiology) applies advanced electrophysiological methods in basic and translational brain research, with the aim of improving the early diagnosis of mental disorders and development-selection of the most effective treatment approaches and schemes. The working group of electrophysiological biomarkers of the disease reported the usefulness of the results of neurophysiological tests in forecasting personalized antidepressant treatment (venlafaxine) and tDCS (reduction of prefrontal theta cordance after the first week of treatment) with functional brain changes associated with response to treatment (eLORETA ROI, linear functional connectivity). The group of machine learning applied the recently developed methods for automatic classification and sorting of polygraphic recordings. RP6 made also a pioneering contribution to the prediction of response to antidepressant modalities [18].

The priorities of the Clinical Research of Mental Disorders program (RP7) are both, research of the neurobiology of severe mental disorders [19] and clinical psychopharmacological trials. Clinical researchers also look for new treatment modalities [20,21]. The main focus of the program is however patient care and provision of healthcare services. Last, but not least, the Translational Neuroscience program (RP8) aims to cultivate a base for applied clinical research (NIMH Technology Transfer Center) and design new therapeutic modalities.

Thus, the NIMH teams working together and with international partners draw a distinctive roadmap of the current and future development of basic and applied neurosciences, especially in the field of psychiatry and related disciplines. With the generous support of the European Union, the Ministry of Health of Czech Republic, and National and International sponsors, the NIMH has proven its commitment to the highest standards in research and clinical care and maturing into one of the leading hubs of neuroscience and clinical psychiatry research in the region.

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