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Cover Story

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The DEEPER Project: Augmenting the Understanding of Brain Disorders

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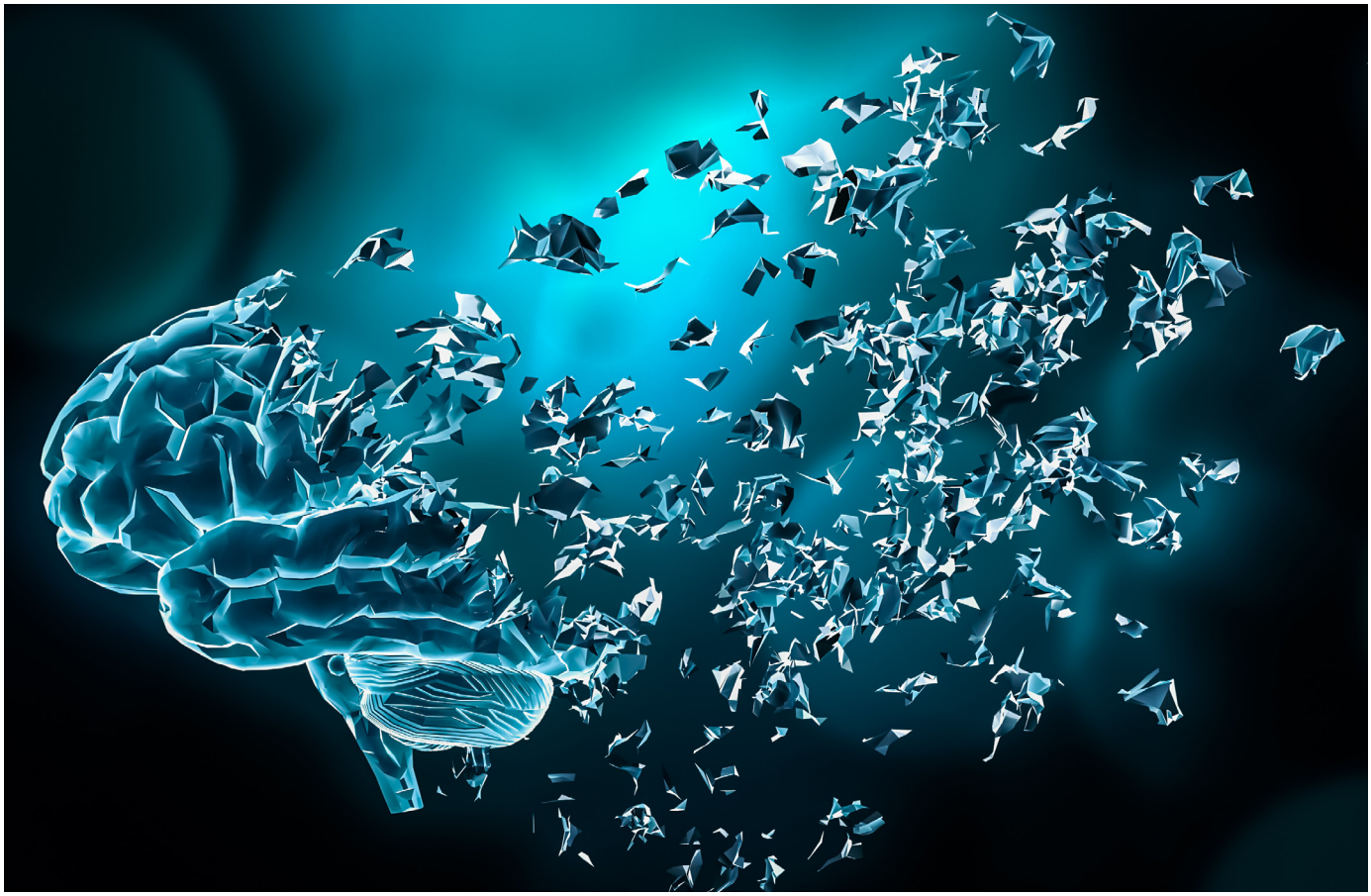
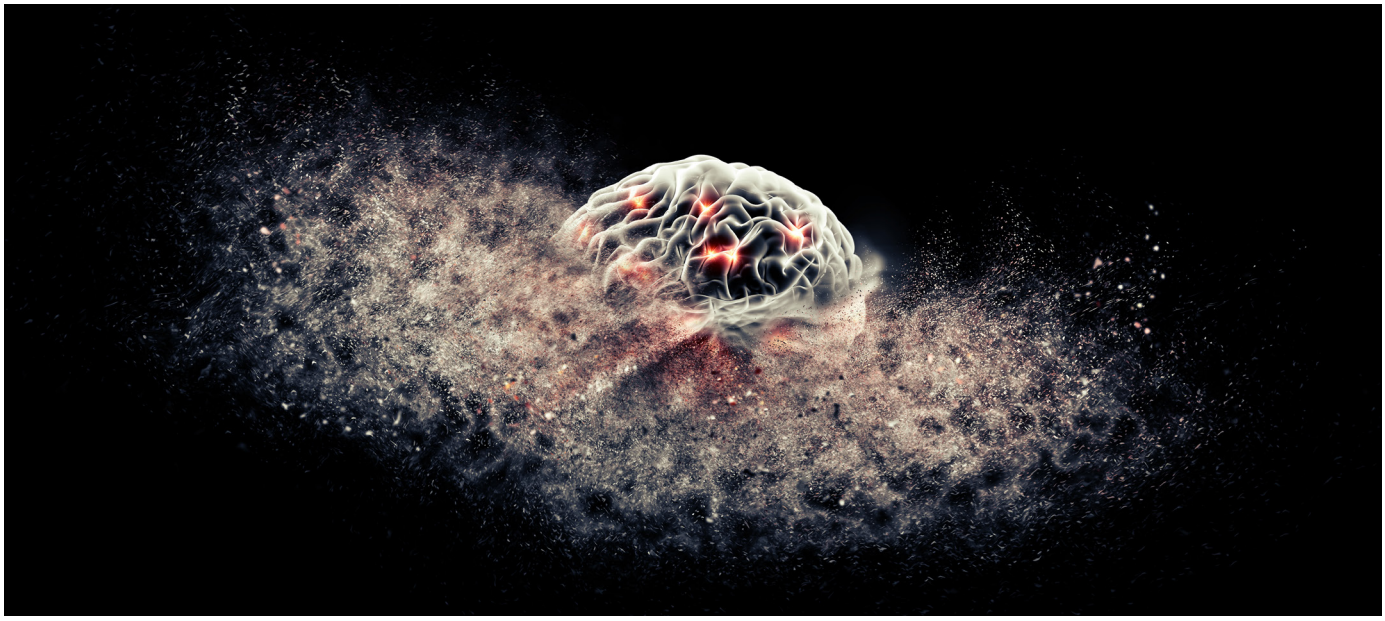
The Deep Brain Photonic Tools for Cell-Type Specific Targeting of Neural Disease (DEEPER) is a unique and ambitious venture putting together technologists, neuroscientists, and clinical experts with hi-tech companies. DEEPER involves 12 partners in 8 countries and is funded by the European Union with about 5.7 million Euros for the next four years. HealthManagement.org spoke to Massimo De Vittorio, Coordinator of the IIT's Center for Biomolecular Nanotechnologies in Lecce, to learn a bit more about this project and the role it can play in understanding and treating brain disorders, such as Alzheimer's disease, addiction, chronic pain, depression, and schizophrenia.





Can you tell us something about the Deep Brain Photonic Tools for Cell-Type Specific Targeting of Neural Diseases (DEEPER) project? Why was it initiated, which primary diseases it targets and what are your primary goals?

The DEEPER project has been conceived because most of the molecular and cellular dysfunctions underlying the origin of several neurological and psychiatric disorders occur in deep brain regions, where current technologies are not very effective. Being not able to efficiently access those regions means that neuroscientists and clinicians cannot fully study neurological pathologies and their aetiology, and validate scientific hypothesis and therapies.

In the last few years, light and photonic tools are more and more employed for studying the brain because they give the possibility to both control and record neural activity with great accuracy and specificity. However, the brain is not transparent to light, and therefore access to its deepest regions with high precision is very challenging. DEEPER aims at producing a wide range of photonic tools to provide neuroscientists the best technologies to face this challenge. The clinical experts involved in the project will target both neurological disorders and psychiatric disorders. DEEPER aims at developing and applying new photonic technology for less invasive and more effective treatments for conditions with dramatic social impact such as addiction, chronic pain, Alzheimer's disease, depression, schizophrenia, and autism spectrum disorder.

The project is a large-scale European initiative that involves 12 partners in 8 countries. What will this collaboration entail, and what role will the different parties play?

The DEEPER project has been funded by the European Union through one of the most technologically ambitious financing systems, the Research and Innovation Action (RIA) on "Disruptive photonics technologies" (ICT-36-2020). The research consortium is coordinated by the Istituto Italiano di Tecnologia (IIT) and involves the University of Zurich (Switzerland), the University of Geneve (Switzerland), the University of Strathclyde (UK), the University of Freiburg (Germany), the University of Hamburg (Germany), the Institute of Scientific Instruments of the Czech Academy of Sciences (Czech Republic), the Sorbonne University (France), the Weizmann Institute of Science (Israel), the Institute for Bioengineering of Catalogna (Spain) and two companies, OptogeniX (Italy) and Atlas Neuroengineering (Belgium).

I am the DEEPER project coordinator, but in IIT two additional IIT principal investigators (PI) are also involved, Tommaso Fellin, Coordinator of IIT Neuroscience Area and Head of the Optical Approaches to Brain function Lab in Genova, and Ferruccio Pisanello, Head of the IIT's Multifunctional Neural Interfaces with deep-brain regions Lab in Lecce. In total, DEEPER sees the involvement of 17 principal investigators distributed among experts in developing molecular tools to make neurons responsive to light, experts in photonic and multifunctional probes for the deep brain, and experts in optical microendoscopy and microscopy. Clinical experts in the already mentioned brain pathologies will guide the technology development and validate it in animal models. This is a unique multidisciplinary team that will enable a study of neurological and psychiatric disorders from different perspectives in order to produce useful technologies for improving knowledge and find new therapies.

There is no doubt that brain disorders affect millions of people worldwide, and the burden of neurological disease is quite high. How will DEEPER help ease this burden?

The discovery of new therapies, treatments, and medical devices to cure and control brain disorders requires first a

full understanding of the origin of the dysfunctions. This challenge demands large-scale initiatives such as DEEPER to face the disorders from both the technological, scientific, and clinical points of view, being ready to immediately transfer the results on the market.

DEEPER is a unique and ambitious venture putting together technologists, neuroscientists, and clinical experts with hi-tech companies. We all share the target of developing new, more effective photonic tools for the brain, and we are all aware that this will enable in the medium/long term effective treatments for multiple neurological pathologies.

How will DEEPER augment the understanding of brain disorders? How does it work exactly?

The possibility to interrogate and control deep brain neural circuits with sub-cellular resolution relies on the parallel development of high-efficiency molecular tools and high-performance hardware tools, i.e., implantable probes, micro-endoscopes, and microscopes. The molecular tools are being designed to make neurons sensitive to light and to produce light in response to a specific neural activity and neurotransmission. This allows a precise optical monitoring, control, and pharmacological reproduction of neurotransmitter transients in the living brain. The hardware tools, instead, deliver and collect light in the deep brain regions and, together with the molecular tools, allow both to acquire images of specific deep brain areas and to control brain electrical activity on selected portions of the central nervous system. The combination in DEEPER of state-of-the-art molecular tools, new minimally invasive probes, microendoscopes and microscopes represents a unique toolset that allows studying dysfunctions at the molecular and cellular level in a very controlled fashion.

If you were to list the key benefits of this project and the technologies that will be used, what would those be?

The key benefits are multiple, especially from the technological point of view. The most important benefits come from the applied methodology because we are facing the project targets from the scientific, technological, clinical, and market perspectives in parallel. Indeed, the consortium includes among the most expert scientists in their respective fields, and their involvement in a multidisciplinary project guarantees the development of cutting-edge technologies and that the research results will be properly validated. The involvement of companies in the project will make sure that any technology result will be immediately transferred to the market and made available to the scientific community. Last but not least, all the developed technologies will be useful not only for the pathologies we have mentioned but for any brain or body region where imaging and photonic tools can be applied.

The tools are believed to be minimally invasive but overall, how safe will these technologies be? How do you plan to test its safety and effectiveness, or if you already have, what are the initial results?

Safety and effectiveness are extremely important both in the short term when validating the technologies in acute and chronic in-vivo experiments and in perspective for their translation in clinical trials. This is the reason why we target hardware miniaturisation and why we are designing and developing different molecular tools whose safety profile will be definitely assessed. However, the DEEPER technology is also expected to be extremely useful in validating the effectiveness and safety of drugs and therapies in animal models, without the necessity of being directly applied in humans.

The project intends to transfer the technological results from laboratory to market. What would that entail? How close are you to doing that, and what does this process involve?

There are different levels for the transfer to market of the project results. The first relies on the presence of two companies, OptogeniX and Atlas Neuroengineering, producing minimally invasive brain probes and whose current customers are mostly the neuroscience labs. This will ensure that the DEEPER technologies on implantable probes will be made immediately available to the scientific community, with an exponential increase of the experiments and impact on several brain disorders. The targeting of the right deep brain circuits and the possibility of understanding the origin of specific dysfunction in brain disorders will enable, in the longer-term, more effective drugs, therapies, and medical devices.

What is your outlook about the technologies that are to be used and the overall goals of this project?

I think that the technology to be developed in DEEPER will have a strong impact also out of the project borders. I expect that all the demonstrated tools will enable a large number of experiments for multiple pathologies and that they will have a huge and lasting impact on the discovery of therapies and on the control of brain pathologies.

Conflict of Interest

None. ■