



Editorial

Future coordination and integration of the results of the EU funded projects on schizophrenia and other mental disorders

On the 15th–16th of June the “Workshop on Schizophrenia and other mental disorders” was held in Pisa, Italy <<http://agenda.infn.it/event/WSMD2017>>. The aim was to showcase the latest developments of EU-funded research in the field of brain imaging tools for mental disorders (diagnosis, monitoring and management) and to explore the research and innovation challenges to be addressed for advancing the field.

The Workshop brought together investigators involved in collaborative research projects funded by the EU through the Seventh Framework Programme (call HEALTH.2013.2.2.1-2: “Development of effective imaging tools for diagnosis, monitoring and management of mental disorders”) and the “Innovative Medicines Initiative”. EU-funded projects on neurodegenerative diseases were also represented to gain a broader view on the state-of-play of brain imaging tools for brain disorders. The manuscripts of this special issue are based on the talks presented at the conference. The Workshop was organized in collaboration with the European Commission Directorate General for Research and Innovation and the EU Joint Undertaking Initiative “Innovative Medicines Initiative”, and was under the patronage of the European Psychiatric Association. More than 120 participants attended.

The Workshop was concluded with a roundtable with selected panelists who discussed how to best address challenges and needs identified by the attendees during the event. The participants to the panel, Lara Passante (Scientific officer of research and innovation for neuroscience, European Commission, Belgium), Elisabetta Vaudano (Responsible for the neuroscience area, Medicines Initiative, Belgium), Jan Bjaalie (University of Oslo, Norway and Leader of the neuroinformatics platform of the Human Brain Project) and Nikolaos Koutsouleris (Department of Psychiatrics of LMU Munich, Germany, and coordinator of the PRONIA project) were moderated by Marlies Dorlöchter (Program Management of the Agency DLR, Germany). The discussion was declined in the form of Q&A sessions. Three specific questions were presented and answered by the panelists, and discussed by the attendees.

The two guest editors’ take home message and critical interpretation of the discussions around these questions are reported below. These are the opinion of the guest editors and do not reflect any direct statement or opinion of the panellists or of their organisations.

1. What are the actions needed for integrating the results of this workshop in a unique successful platform?

If one looks at the future, and in particular at personalised medicine, s/he has to address diseases/disorders by three main actions: detection, interception and treatment. Therefore, the following questions were proposed to panelists: how do the contributions to this Workshop relate to these three actions? A lot has been said about technology and biomarkers, but what is a biomarker? What do we want to do with it?

If we consider the perspective of patients with schizophrenia, they are people with different family situations and a group of symptoms that are quite distressing. They ask the clinician what is going on and the clinician asks herself/himself which diagnosis is appropriate for this cluster of symptoms. Moreover, when a technology is used which introduces a risk, the patient wants to know what type of risk and what’s the advantage of taking the risk. To achieve a successful platform, the most important thing is to implement a good communication, so as to streamline the transfer of information from researchers to clinicians and from clinicians to patients. Secondly, highly performant predictive models are needed. Third, the operational conditions must be clear and well defined. For example, a clinician should know whether a specific biomarker is useful in a certain condition.

It was outlined that there are already active platforms, such as the personalised medicine branch of the H2020 framework programme. It is important not to forget aspects such as inclusivity and accessibility of the services. It is necessary not only to translate the technology to the clinics, but also to support and facilitate its adoption. The European Prevention of Alzheimer’s Dementia (EPAD) project is an example of a success case. The EPAD aims to deliver a clinical trial platform for secondary prevention of Alzheimer’s disease, i.e., preventing the development of symptoms after the onset of the disease. This project has been facilitated by Alzheimer Europe, a very active organization that supported dissemination and communication. Most remarkably, this organization supported directly the project coordination, by participating to the steering committees with rotating representatives. In addition, the project produced new skilled personnel able to work at the interface between technology and clinical procedures, who is eagerly sought by the industry.

Longitudinal studies were mentioned several times during the workshop: there is a general consensus on their importance in clinics and on their need for a platform where data is guaranteed to last long enough. In fact, technology cycles normally make data obsolete after a while, despite the fact that old data still retain their value. To improve this situation, we need some plan on sustainability. In order to achieve it, a system that can provide support along the whole course of the study would be highly beneficial. This cannot be done in a project with a lifespan of only a few years. Therefore, we have to consider longer funding schemes based on dynamic/re-modelling platforms, such as a *European Research Infrastructure* that can provide a series of integrating activities comprising trans-national access to the data, networking and joint research for the psychiatric community. Whatever is the platform, it should include patients: it is possible and it would not hamper research.

The problem was raised if there is the willingness to share data and samples. The data, to be sustainable, should be research-driven. The problem should be tackled by government bodies but no one is moving towards providing infrastructures and resources for patient open data. The importance of metadata was also emphasized: correctly organizing metadata is part of the challenge of making data sustainable. Sharing data would mean sharing models: this requires data standardization. Standardization and sharing of instrumentation is an extremely important issue to be addressed by the instrumentation community. However, the Intellectual Property rights should not be put to danger, otherwise researchers won't share it. Data competition framework is an example of sharing platform where researchers can share their models safely and without risking to lose the corresponding revenues.

2. What are the most important topics to be considered and the most relevant steps to be taken by the funding agencies to implement a successful “Brain diseases and mental disorders initiative” for the next 10 years?

In the context of the overall environment in which we operate (policy, regulatory, the next Framework Program), a balance should be found between existing and emerging societal challenges and the needs for the research community. As for IMI, that funds collaborative public private consortia focussed on tackling challenges in the development of novel medical treatments, the community has to discuss and produce evidence that there is something of value worth to be studied. For funding agencies, it is extremely important to have a continuity in getting the fruits of research.

In order to stimulate bottom up research, researchers would need clear statements on what are the open questions, or the missing parts to understand and tackle today's societal challenges. What is needed is a vision that describes the continuity from basic research to implementation. There is no obvious stream, there are many ways and many missing dots.

The importance of the true meaning of phenotypes was discussed. One should not forget that a phenotype implies that there is genotype of which it is an expression. In actual facts, the phenotypes we are talking about are pretty arbitrary. Their definition comes mainly from a few individual institutes or organizations, e.g., such as in DSM IV or DSM 5 and ICD 10. Therefore, we have the presumption that there is a phenotype hoping that a genotype will be identified and will point to a meaningful etiology. However, so far this model has not been very successful. Therefore, we should consider the possibility that the whole approach is wrong and different conceptualizations and research frameworks are needed.

It was suggested that biomarkers might not be relevant to existing mental disorder categories: a biomarker might be unspecific due to

the overlap of symptoms in different disorders. The following topics were also stressed: the usefulness of lobbying for achieving a larger consensus on the importance of research in mental disorders, the importance of animal models and the importance of understanding human brain ageing.

It was reported that the EC is now working on defining FP9. The EU has put a reasonable amount of funding for the Human Brain Project, while the Chinese counterpart is going towards standardization, by creating two huge facilities dedicated to brain research. Everybody agrees that the current discussion could be important in defining what are the specific topics that needs to be launched in FP9.

3. What would you suggest so as to increase the synergy between clinicians and scientists?

During the workshop, it was interesting to see how the various groups presented different ways to pursue the search for possible biomarkers. Developing biomarkers requires a certain set of qualifications, rules and capacities. Regular meetings between clinicians and scientists would be helpful in coordinating these different efforts. In general, more interaction would improve research in general. A recommendation came out of the discussion: projects should have both clinicians and scientists on board, as suggested by several success stories with such a configuration. However, if it would be easier to achieve this at a European level, it might be more difficult at a national level, because of the distrust and inertia of the academia in many countries.

The panel also recommended initiatives aimed at enabling young researchers from different groups to meet and discuss together, to expose them to different challenges in various projects. This would require a certain standardization of postgraduate education. Marie Curie fellowships are a good instrument, but they should be improved in the direction of interdisciplinarity. The EC is trying to encourage the interdisciplinary aspects, without broadening too much the topics This synergy would be fostered further if the bar for accessing research were lower. Today it is too difficult to get projects funded. It would be wiser to give more numerous “but shorter in time” funds and then follow up on the best of them. It was agreed that the success ratio of H2020 collaborative projects is rather low, due to the kind of topics which are very prescriptive in the approach, but also because of the limited budget.

The paramount importance of the reviewing process was stressed: a reviewer who is not an expert in the topic will never give the maximum grade to a project, but there are topics where there are not many expert reviewers. The funding agencies should address this problem to find the suitable reviewers, also extending the search to young scientists, who have to be carefully selected and informed. This is a complex task, but there is a great emphasis on doing it at its best. It was outlined that the EC is always looking for good reviewers, and everybody in the audience was invited to register as a reviewer in the EC portal.

Key points of the panel discussion are summarized hereafter:

- Find a communication model to streamline research information to clinicians and patients, to share and keep patient data safely and effectively
- Find a sustainability model for keeping long term research-driven data
- Support bottom-up research by conjugating the societal challenges into clear statements on what is missing and what are the open questions
- Consider new research strategies in which the biomarker diverges from the current phenotype/genotype conception in the understanding of brain and mental disorders

- Search for a new interdisciplinary education model and promote the exposition of young researchers to different scientific communities
- Enlarge participation to research by easing the access to funding and supporting the most successful outcomes

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Available online 1 February 2018