

Minutes of Workshop on the European Population Neuroscience Strategy  
20<sup>th</sup> of November 2015, Brussels.

10.00 Welcome

**David Nutt – President of European Brain Council and Professor at Imperial College London**

- One third of the population will develop a brain disorder
- The societal costs related to each disorder are enormous
- Our knowledge about each single disorder and processes is very limited
- The industry is passive towards investment because of low success.
- We need new European approaches to obtain new knowledge and we need more research on each disorder
- Each disorder can be subdivided into several sub-diagnosis
- Can we use the power from brain imaging in defined large populations to improve diagnoses and treatments
- Today we take the first step!

10:05 Setting the scene

**Thomas Werge – Clinical Professor, University of Copenhagen**

- Local scale studies may direct us to study end points rather than processes
- Investigate the development of large populations. Global picture of patients and disease pathways are necessary. It is time to move from local scale to global scale - Size matters
- Europe has led disease genomics for years and we have learned to share data, but other countries are also launching new initiatives
- The lessons learned from genomics can be used in neurology
- How can we protect people whom research finds to be predisposed to disorders?
- Denmark has (by coincidence) collected blood samples from all newborns for almost four decades.
- Can we create a reference brain similar to the reference genome that is used in genomics? And will a reference brain be representative for the European/global population? Probably not!
- Continue to study the brain and find the boundaries of what is supposed to be “the normal brain”

10:15 European population neuroscience: impact, opportunities and challenges

**Hartwig Siebner – Professor at the University of Copenhagen and Head of the Danish Research Centre for Magnetic Resonance**

- 35% of all disorders are brain disorders
- Only few people will go through life without being affected by a disorder
- Human development is affected from both genomic and environmental factors throughout life
- There are three “-omes”: *The GENome, The PHENome, The ENVIrome*
- Phenome: the interaction between brain and body is important – embedded environment. There is already a lot going on in Europe. The Human Brain Project is complementary to “this” but is not the same.
- Neuroimaging can go a few steps deeper in phenotyping
- Long term following citizens and patients. How can we follow individuals over long term in sustainable ways? The funding systems favour short term projects, often PhDs do the studies, then leave.
- Longitudinal sampling – over time is difficult
- Genetic, environmental & socioeconomic factors render human brains and the behaviors they produce remarkably diverse. Collecting Multi-Level BIG-DATA: ‘-Omics’, neuroimaging (MRI) and sensor technologies permit the capture of diversity in the population with unprecedented precision. Leveraging these technologies in decision making will help to realize personalized treatment.

- The time is right: Advanced genetics (WGS – spell out), emerging technologies, advances in handling and harvesting BIG-DATA
- Smart sampling
  - o 1. -> What is a representative cohort? Who will participate -> are they representative for the population -> probably not. How do we access the people that are difficult to reach?
  - o 2. . Data issues – what has to be accessible, who should have access, and how open should it be etc.
  - o 3. Bias participation – how do we actually reach the whole population? (And not only the ones likely to participate in studies)
- How do we make a business case of data – open access – how do we share?
- Mission to identify and detect trajectories to get people back on healthy ageing track
- The precision medicine initiative. Catch up upon what is happening in US or China -> they will not do the work for us.
- Multinational-population-based large cohorts, including lifetime studies. There is a need for more longitudinal sampling running for several decades
- Prediction and prevention is the main goal → Citizens benefits: ~~prediction and prevention~~, boosting industrial innovation, development of intelligent solutions – personalised medicine, access to individual data for patients and citizens.
- Many challenges -> one is the methodological -> We must look and identify all variables-> small scale studies might make the wrong conclusions.
- We must do our research on different levels: symptoms, neurology etc. and start mapping the “Brain Phenome”
- We must study both exposures and outcomes
- Strategy to bring Europe together and create a Brain-centered library.
- Why Europe: Unique strength and possibilities -> We do not need to reinvent the wheel, We have already shown that we have the competences, Capitalize on the diversity we have in Europe, Creating the Framework -> ethical, legal, data sharing,
- Imaging – a lot of modalities, MRI is upcoming technology to create a pipeline. Can be applied at European level. Still under development. Other methods are difficult to apply to the brain.
- Imaging – a lot of things are going on. Registries in several Scandinavian countries , Human Brain Project is complementary. Europe is diverse, important to capitalize on this diversity
- **Propose – European population neuroscience strategy. Multi-national population level. Life course important but challenging.**

### 10:35 EU Perspectives

**Robert Madelin – Senior Innovation Adviser, European Political Strategy Centre**

- A global challenge at all age groups
- How will your vision of a data library interact/comply with other projects?
- Challenge to join up with other projects
- Diversity needs to go beyond Europe –compare with other regions.
- The Human Brain Project Flagship... -> There is complementarity between the flagship and where you want to go
- To give flavour of the landscape. Other initiatives than Horizon 2020 focusing on brain disorders, (IMI, JPI, Human brain project). Complementarities between existing things and what you want to achieve. Need to challenge ourselves to be truly joined up to other things. To really link activities to each other

- Different actors should be in from the beginning. The business case should evolve in parallel with the research. If business and investors are not in they will not be part of the talks. The business case is best when the market is global. Can we partner with representative populations, e.g. China, Brazil, South Africa. It would strengthen the case.
- Brain science should be plugged into platforms that already exist or are under development. Diversity of populations is very important.
- Obesity research is an example where a lot of knowledge is generated but it doesn't produce solutions. E-health and m-health communities who would like to play with the available information.
- Mental health wellbeing strategy was suggested in 2006-2008 to the Barosso Commission. The result was the JPND. Fix the bad thing rather than work on positive messages. Wellbeing argument is not easy to sell politically.
- We have many projects (thousands going on -> 1931 ->FP7) -> What makes your project so special?
- Other fields of European research try to argue the same case. You come down to the common platform, access and rights questions, high performance computing stuff etc. The winner will be someone that comes up with a system that can be used for a common purpose.
- Skip the fortress around Europe case -> we must lead but also collaborate. Proactively partner with populations/countries outside Europe.
- How to apply tools; how do we comply with new developed methods, how do we harvest; the things we create must be interesting to other partners -> make it interesting so that people not used to work with neuroscience wants to work with neuroscience although they don't know anything about it.
- We start with a problem (brain disorders), we talk about negative things that we want to avoid, but we fail to emphasize the good things that are going on. Let's have a strategy that focuses on full potentials, focus on good things we can achieve and not bad things we can avoid. Moving in a landscape with 1000 projects and large investments in research. Midterm review of budget and of H2020. Couldn't launch more FET flagships due to budget restrictions (gap between Commission proposal and Council agreement on budget).
- All the things we are saying should be immediately familiar to the people that need to be in.
- BBMRI stakeholder group on how to use ICT, data – too much data. If we want to connect genetics with genotype, phenotype, we need quality data. Open data has two different levels – data useful for public health, on the other hand you want data that is very individual. Patients stopped giving data. Losing trust. Take care of the changes across the world where research doesn't own the data anymore. IP of data will be more shared than before. It needs to be taken into account when planning research.
- Brain disorders: diseases we want to avoid – but what is the good things we want to achieve? We want a strategy of what full potential of the benefits that can be achieved!!!
- EC: Idea – personal account – patient who take part in the “studies” and see the benefits give continuous consent. Not just nice to have – is essential.

#### SESSION DISCUSSION

- Has previous collaboration in consortia been successful?
- Other existing initiatives have similar aims compared to this project. It all comes down to the same platform (it is the way the world is going)
- The best project is the project that is able to come up with a very broad and general purpose – e.g. like a computer.
- Add this approach on other approaches that all have a more general approach.

- Be aware that small collaborations in some cases are more agile and able to obtain better results in shorter time. Keep collaboration on small simple and effective units but as part of larger consortia.
- Remember to include the positive outcome. Research on brain disorders will not only prevent the development of disorders but it will also “make better brains”.
- The library is a good idea and should also include and combine already existing data (there is tons of available data that just needs to be combined). It is possible that there is too much data available and there is a need to select among the quality of the data.
- It may be a challenge that participants will stop sharing their data if it gets too personal. There is a growing awareness on, what is happening to the data. A possible solution could be to keep two copies of data. One with the participant’s name, which can be used in collaboration with the doctor, and an anonymous version that can be used for research. We must continue to advocate for thriving and be creative when selling the arguments to participants. The well-being argument is not easy to sell but it is very much needed.

### 11:35 First Panel – a European population neuroscience strategy

#### **Dr. Tomáš Paus – Anne and Max Tanenbaum Professor and Chair of Population Neuroscience, The Rotman Research Institute and Professor of Psychology and Psychiatry, University of Toronto**

- Population neuroscience combines Genetics, Neuroscience (imaging) and Epidemiology in thousands of individuals.
- It is relatively easy to obtain the –omics and imaging data but far more difficult to obtain data capturing the wide variety of social and physical environments (epidemiology).
- Information and Communication Technology (ICT) will be the answer to this challenge (data about social and physical envi.). Smart phones, social media, etc. will be used at individual and aggregate levels, innovative sensors (e.g., physiological monitors) at individual level.
- Scanning is a versatile tool for obtaining large amount of quantitative data. It takes about 90 minutes to scan the entire body (brain, cardiovascular, body composition).
- There are 503 million EU citizens in 28 countries. There is a need for an efficient and high quality plan for collection of data.
- Set of cohorts. Cover the whole life span (5-10 year longitudinal cohorts staggered to cover full lifespan – from 5 to 90 years). When possible, embed new samples in the existing cohorts. Establish 20-30 such cohorts, each including 3,000-5,000 participants (a total of ~ 100,000 participants across the lifespan and EU).
- Global Alliance for Genomics and Health. Data working groups. This is an example of existing organisation that is already solving relevant issues (e.g., ethics, data protection, data sharing).
- Need for high quality data that is easy to access from omics side. Imaging technology already works very well. Need to see how to couple with epidemiology (social and physical) environment) in the most efficient way.

#### **Dr. Daniel Pasini – Human Brain Project Flagship (HBP) DG Connect, European Commission**

- Human Brain Project – try to present the angels where there is overlap. Multi-disciplinary – more than 20 countries all over the world. Scientific roadmap of ten years – 1 billion. We want to create synergies with national initiatives.
- EU, US, Canada is involved in the project. 50% funding through EU, member state funding to create synergies. HBP builds up relations with other initiatives around the world.
- Aims to understand the human brain and ultimately seeks to emulate a computational model of the brain and model the neurology of the brain.
- To build an integrated ICT infrastructure – six platforms for neuroscience, medicine and computing. To build biologically correct models of the brain.

- Paradigm shift in neuroscience and open data. Data integrating project. Need to produce data too – mouse and human brains. Cognitive neuroscience, analysing in detail the functions.
- Building a scientific infrastructure which will be open to communities. Pushing super computer to treat data.
- Building new devices inspired by knowledge on the brain.
- The Human Brain Project is building facilities for neuroscience research, brain medicine and computing. The Human Brain Project has the potential to become the central hub for accessing large quantities of neuroscience data.
- Neuroinformatics platform is linked to what we want to do. Alliance with Allen institute for brain science. Many international initiatives have been developed in brain research – us, Japan, Korea. Cooperation with these initiatives is important.
- Medical informatics platform – linkages to hospitals to access hospitals data. Negotiating with hospitals across Europe for them to get involved as testing facilities.
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**Dr. Catherine Berens – Head of Sector Neuroscience, DG Research and Innovation, European Commission**

- Make use of what already exists; pools of data and infrastructures. Ongoing reflection in European Commission, how to use data and how to link with JPI and IMI. Involving industry. Relevant IMI project following people at risk of developing Alzheimer's.
- Would it be possible for us to come up with some sort of standardized tool? Ongoing issues. Initiative with US and Canada around traumatic brain injury. How to collect the data, ensure quality etc. to identify most effective clinical interventions? MRI is a very important tool, it is discussed how to standardize it.
- There are many opportunities under the H2020 program, including funding of multidisciplinary approaches. Emphasis should be on how to maintain health, not just diseases.
- There is no one-size-fits all. Make sure that all resources can be put together.

**Dr. Ali Sarem-Aslani – Director of Clinical Research and Innovation, Medtronic Neuromodulation Europe**

- Companies will only engage in research if they can see it as a potential investment.
- Failures on research investments are good, if we learn from them.
- There is a need for an innovation ecosystem that supports companies' engagement in research and development. We can only face the challenge in a system with many partners.
- Companies have in general enormous expenses in research. Industry has failed in Alzheimer's research, has burned billions of dollars in that area.

**Dr. Adam Hampshire – Senior Lecturer in Restorative Neurosciences from the Imperial College London, ENCP Imaging**

- Great potential in using the technologies that people have in their homes, personal devices. We can reach a high population group, cheaply and over long time.
- Patients enjoy training session, high compliance.
- Put more emphasis in utilizing the technologies that participants have at home. It has the potential to revolutionize the way we study cognition – Testing in the clinic vs. testing at home. The potential in testing people at home using their own computers and other devices are huge.

**Moderator: Hartwig Siebner – Professor at the University of Copenhagen and Head of The Danish Research Centre for Magnetic Resonance**

## SESSION DISCUSSION

- Intervention: How much can intervention help?
- How can we implement into what we have?
- How can we plugin into existing databases?
- Hartwig: Add-on to the Human Brain Project (HBP) would fail our project, but it may be possible to enlarge the scope of the Human Brain Project. HBP is very distant from what we propose – we are longitudinal, we engage more with the society, and are interested to find out what shapes the brain through life. I envision it as an potential add on to the HBP project
- Daniel: Important to map what is already done. HBP is providing resources that might be useful for you – you can work with them. We do not want to enlarge the scope of HBP but we need to cluster. Could work further with you.
- Thomas: HBP is a platform. We are talking about content. Neuroscientists cannot create it alone. Population studies are coming in. The focus should be on the population level, not individual. Data collection needs to be done at individual level on a very large scale (+100K). However, otherwise we will never understand the complexities. Need to couple external environment with individual data. Exploit cohorts efficiently. You have to start from scratch – data sets from different initiatives are highly heterogeneous, collected with very different mind sets and starting points and therefore not easy to pool and combine together.
- There is a need to include more skills and disciplines into the process. The process should neither be disease driven. The success will be lacking from only putting existing projects together. Further, one should be aware of future use of the data that will be collected – None of us can foresee how data will be used in the future. By coincidence Denmark initiated a process of collecting neonatal blood spot around 1980. Today this has developed into becoming a unique genome library. This strategy should also be used in the future.
- It is important to recognize that diseases start long before patients go to hospital.
- Register data will play an important role and it will be a challenge to link population data. Important not to ignore what is already there.
- There is massive amount of data present but what is lacking are platforms and infrastructure.
- Hartwig: Prospective approach. Explanatory retrospective studies do not necessarily provide us with the correct information, there are plenty examples of where these have failed. They are important data sources but are not going to predict the future. Omics need to be included.
- Caroline: Data needed in order to develop analytical tools, discussion about the usefulness of existing data. Solid potential. Very crucial to link with all communities.
- Thomas: ICT in HBP. Huge ICT in global alliance for data health. Interoperability is key word. But it is not working. ICT people need to do more for interoperability. User needs to be involved in developing interoperability. Data base designers and managers should work closely with medical people.
- It is important to develop a platform and link it to all resources, including the Human Brain Project. If we don't do so we will end up with a platform that does not answer our necessity.
- How can we deal with former mistakes and be sure not to repeat the same mistakes?
- What can we do to deal with ICT systems?
- Recruitment and involvement of participants from the beginning is a game changer. Use ICT and the information that already has been collected. Get back to participants with the information that will be useful for them and make them want to participate (non-pharmacological intervention with benefits). Educate the public about real meaning with deep science.
- It is important to reflect the usefulness of biomarkers and other results for the next level and for the participants.
- It is a common mistake to compare healthy and diseased participants. It is better to switch over to longitudinal studies.

- Arno: What to do if the money was there. Thomas: Establish one cohort per country; 28 cohorts. One scanner per cohort and sampling different age span for each cohort. Harmonize before/during the study. This will make us able to provide the Human Brain Project with the information about what shapes the brain, which is the insight that the Human Brain Project in itself does not provide.
- Salam: Interventions and perhaps early interventions also have to be included in the discussion. How can you shift the big data to information and how can it be transferred to clinical interventions.
- Thomas: started using ICT in generating information, quantified self-approach.
- Caroline: Making sure that even early stage research also informs later developments in interventions. Researchers should not work in isolation. At some point others need to take over to move forward.
- Thomas: Mistake to compare healthy people with sick people. Need to work at population level.
- Robustness of data comes from the big number of population data.

### 13:35 Second panel – implementation of a European population neuroscience strategy

#### **Dr. Amalia Irina Vlad – Head of Sector, DG CONNECT, European Commission**

- H2020 offering a lot of opportunities that are developing now.
- There are multiple of similar projects running and this initiative will not be built on empty territory.
- Important that a strategy has a complementary approach and relate to existing or previous initiatives.
- The commission finds brain research very important and there are initiatives in the 2016/2017 call that are in line with this approach
- There will be given priority to high-performing computing.
- HBP and ERA-NET coordinated with MS. Most MS want a new ERA-NET on neurology.
- Communities are not isolated but collaborating.
- You need to take into account other sciences. The key to success in H2020 is multidisciplinary.
- Personalization, wellbeing, prevention, integrated care, not possible to plan research without coupling neuroscience with other disciplines including social sciences and humanities.
- Data integration, in silico development and testing. Topic on resilience and recovery – in line with what you want to do.
- Privacy is highly important when implementation has to be done.
- The infrastructure is an important issue for the Commission. ICT has a special role in that.
- ICT holds the possibility to combine large amount of data.
- A number of platforms capable of handling data on health already exists.
- Several aspects on data – waiting for data protection directive to be adopted in 2016. Create issues for quality of data.

#### **Marc Lange – Secretary General, Representative from Health Telematics Association**

- Telematics is a multi-stakeholder.
- E-health is available everywhere but not to everyone.
- E-health should be implemented but policy makers make different decisions around Europe (Every Member state has its own agenda.).
- E-health holds the potential to move a great deal of care from hospitals to private homes.
- E-Health is using ICT for the course of providing healthcare.
- Mobile health is an additional term.
- E-health, telecare and self-management go hand in hand.

#### **Paul Arteel – Executive Director, Global Alliance of Mental Illness Advocacy Networks-Europe**

- It is important that patients get involved actively in research projects.
- Patients would like to be active participants instead of being objects of enquiry.
- It is important to respect the experience and expectation of the patients.

- Patients should be involved and disseminated – it doesn't make sense that researchers are writing reports and scientific dissemination which aren't accessible for the patients.
- It is very bureaucratic to be involved in research projects, European Commission is administratively heavy.
- There is a tendency towards that results are always presented as a comparison between countries. Research should be done global so results are valid globally.

**Ann Little – President, Representative from European Federation of Neurological Associations**

- There is a movement from patient as passive to becoming more involved - they can contribute regarding privacy of data, ethics etc.
- Without the patient there is no data.
- How can data harvested today be used in 20 years?
- Patients need full control over use of data, how long it is kept etc.
- Each patient's personal data is very valuable for them self. For instance, many people are reluctant to allow insurance companies to get access to data.
- Stigma is very important.
- Big data is important in rare disease areas. Without it you cannot get the data that you need across Europe.

**Moderator: Torsten Ringberg, Professor, Copenhagen Business School**

- Tomas Paus: Active participation and active participant consent, very important to the data we are talking about now. Telemedicine applies directly to what we are talking about. Information gathering directly from patients/citizens. Active action from patient contributes to data gathering.
- It is possible to continue to do neuroscience research without the consent from patients, but with consent much more data (social and behavioral) will become available.
- Paul: Patients are very happy and cooperative relating to technology. Health care professionals do not cooperate around technologies. They are reluctant to include patients.
- Most data requires consent from the participants and participants would like to become actively involved.
- However it is a problem that participants have not been explained in layman language what is going to happen.
- Comment: We talk about clinical and basic research.
- William: It is about understanding the developmental pathways – before people get a disease. This is important if we want to be able to predict, define public health policies and preventive programs.
- The border between being a participant and a patient can easily be crossed due to accidental findings, which needs to be taken into account.
- Tomas Paus: Population based approach is about community based sampling. At the end, a representative sample will consist of conditions that are represented in the population.
- It is important to involve patient organization in relation to deal with this matter. Population based cohorts should include everyone, and not have any exclusion criteria.
- It is possible to recruit huge populations for research projects by going directly to participants
- Participants should be able to choose to be informed about findings under certain circumstances – Accidental findings are to be presented and evaluated by an independent expert board before the findings eventually are presented to the participant.
- It was suggested to let specialists rewrite researcher's results into layman language to make the outcome accessible to participants.

- William: It is important to move towards talking about the overall objective, the common goal we want to achieve and which can unify all stakeholders including citizens. If one finds common ground, issues that separate different stakeholders can be easier dealt with.
- Next step: Become more transparent and focus/talk across borders.
- Agree on which idea is good.
- Include an altruistic approach and look at projects in a longer perspective: Start gathering and providing the data for the high-impact papers that will be published in 20 years from now. It is important to trust the ideas and be able to share with other participants.

#### 14:35 Concluding remarks

##### **David Nutt – President of European Brain Council and Professor at Imperial College London**

- The project has to span the whole life, and include genetic analysis, environmental analysis
- Genetic sampling is easy; technology is there, environmental sampling will be more challenging.
- Europe has the potential to take the lead in this matter but projects and initiatives must also link outside Europe. Diversity will add to the strength of research excellence in Europe.
- We need to be aware of fast advances in other areas, e.g. global health alliance (mentioned in the presentation of Thomas Paus).
- We must consider existing cohorts that are being funded by DG RTD. Daily we just do our own new cohort. Must make best efforts to find out what is available. That would mean talking to HBP about e.g. data sharing.

##### The first practical steps:

- Access existing cohorts in Europe, e.g. UK (e.g. ALSPAC 20+ year developmental cohort in Bristol,) Finland and Denmark and select the best cohorts and use those to convince national and international funding bodies to support the idea.
- Collaborate with the Human Brain Project on data sharing.
- Look at the best ways to measure environment
- Explore the possibilities to do brain test etc. in participants homes
- Make the public to become interested and bring in commercial people with expertise in developing technologies
- Formulate a discussion document to be discussed on the next meeting (1½ day)
- Approach the Wellcome Trust and Lundbeck Foundation (interested in optimising the use of cohorts).
- Bring in more people from more diverse backgrounds.
- Meeting in Copenhagen, probably July.
- Steering group to plan the conference.

##### Stakeholders e.g.

- Data protection and Justice
- Big Data
- Pharma companies
- Health business
- Scanner people (incl. companies)
- Patient/citizen representatives (there is a need to change the public view on health research)
- Social science (maybe Ann Borges, sociologist)
- Ethics

Next stage discussion document by February. The document should be endorsed by the European Brain Council because it will give it more weight, 1 meeting early next year.