European Parliament Interest Group on Mental Health, Well-being and Brain Disorders

Meeting the need for improved treatment of brain disorders

2 June 2015

Nessa Childers MEP welcomed participants and reminded the audience of the aims of the Interest Group, i.e.*to advocate the development of sound EU policies which contribute to prevention of mental health problems and ensure good services, care and empowerment for those affected by mental health problems.*
She then introduced the specific objectives of the meeting, i.e. to be informed of the need for improved treatment for brain diseases and mental health, to hear the views of relevant mental health stakeholders on the topic of unmet needs in brain research and patient outcomes and to have an open discussion on how this topic can be further advanced at EU level.
Mrs. Childers then introduced the first speaker, **Frédéric Destrebecq (European Brain Council)**, who apologized on behalf of **Professor David Nutt**, who could unfortunately not attend the meeting.
Mr Destrebecq first introduced his organisation, which acts as the common platform for the 'brain space', uniting patient, scientific, medical and industry perspectives around a common vision and speaking with one voice for the sector. EBC was launched in 2002 and supports basic and clinical research in neuroscience, fostering dialogue between science and society. One of EBC's major accomplishments consists of mappings carried out in 2005 and 2010 on the cost an burden of major brain diseases; in a major study in 2010, it was found that the total cost of brain disorders in Europe amounted to € 798 billion (publication from 2011[1]). EBC also runs National Action Groups and Brain Councils, 30 of which have been set up between 2011 and 2015. These too advocate for research at local level and provide vital grass roots knowledge, enabling progress at country level.
The second part of Mr Destrébecq's presentation focused on a White Paper, released by the International College of Neuropsychopharmacology in co-operation with other organisations among which EBC, entitled 'Innovative partnerships to accelerate CNS drug discovery for improved patient care'. This Paper is based on the finding that CNS disorders are the understated health challenge of the 21st century, as one third of EU population will develop brain disorders. However, revenues from CNS drugs are predicted to decrease, prompting investors to withdraw their support. In addition, CNS disease research is considered to be the most unpredictable and costly, with a high rate of failure. Hence, the dilemma for investors: while the area is characterised by high unmet need and potential for development, the risks are high. The area of brain disorders is characterised by stigma and non-accessibility to treatment, despite a growing need and prevalence. The cost of treatment is high and waiting times are long, also for reimbursement and approval of medicines. The White Paper was developed to address these issues and focuses on 5 main topics:

1 Connecting Science and Regulation

A better understanding of brain function is necessary and this can be overcome through a closer dialogue between the actors and regulators within the research sector. There are many challenges relating to the high complexity in CNS: i.e. few biomarkers and little molecular definition of illnesses, no clearly defined endpoints and poorer understanding compared to other conditions. Solutions could be found through: collaborative approaches in drug development, improved dialogue regarding how clinical trials are run, sustained communication – unhindered by conflict of interest policies, refined regulatory processes against scientific advances as well as attracting investment in basic and clinical research.

2 Benefit-Risk – Effective research and Implementation into clinical practice

We need to overcome the disconnection between clinical trials and real-life practice: the criteria for recruitment are narrower, and oversights relating to co-medication, adherence or adverse effects re much stricter than in actual clinical practice. It is hence difficult to ensure real-life effectiveness and develop valid

[1] http://www.europeanbraincouncil.org/projects/CDBE/2010/

clinical trials designs. However, innovative clinical trials with clear and relevant endpoints should be developed, with medicines having faster access to market at a lower cost, high quality standards and a more predictable drug development process. Involving patients in trial design could help progress as the outcome measurement would focus on 'real world targets', there would be a better understanding of the performance of a drug, even more so with functional outcomes being included. Ideally, data collection should be patient-centred and facilitated by m-Health or e-Health applications.

3 Knowledge Transfer & Protection of Innovation

What is needed to improve the current situation is the creation of 'co-operative research centres' and set up a platform to organise exchange of knowledge. Such incentives are likely to encourage Academia share its findings.

4 The need for modern 21st century perspective on new tools to assess treatment effects

Decisions by regulators are currently based on tools and scales that were developed in the 1970s-80s. These have never been updated on the basis of the latest scientific insights. Moreover, there are no agreed biomarkers and standardised nomenclature is lacking. This could be addressed by the development of alternative diagnostic tools, such as cognitive markers. A large database will be essential to develop and test, also providing for quality of life measurement.

5 Incentivising investment in brain research

The low Investment in CNS can be explained by stigma and under-recognition of the importance of the area; hence governments and companies do not put this topic on their priority list, despite its clear economic impact (mainly indirect).

There is a need to raise the profile and awareness of these huge unmet needs in CNS and demonstrate the cost saving effect; stronger patient advocacy and joint investment strategy are both required.

Again the patient involvement in trial design and the definition of endpoints would be helpful, as well as large-scale patient registries.

In conclusion, Mr. Destrebecq briefly outlined a proposed EBC-run project that will aim to capture the cost of non-treatment, which is currently being elaborated. Further developments were announced, particularly in 2016.

The second speaker was **Rebecca Mueller (Ups and Downs),** who spoke about treatment, unmet needs and better outcomes from her own personal experience. First of all, quicker diagnosis is key as for most patients with bipolar disorder as it can take 8 to 10 years to obtain the correct diagnosis. There should be a quicker prognosis of treatment success (positive response) with certain medications, as there is a lot of trial and error to find the correct medication; in many cases, patients spend long periods of taking medication with no effect. Psychoeducation and psychotherapy and self-help groups (peer support) should be considered as vital parts of treatment: patients are the expert on their condition and the more the patient knows about symptoms and treatment, the more she/he is in control of the recovery process. The dialogue between patient and doctor is crucial in this respect.

One of the most prominent reasons for patients to stop taking their medication is their side effects. Insufficient symptom reduction and relapse prevention are other reasons for non-compliance; there should be more different medications to enable more treatment options.

Treatment should be seen as holistic and serve to improve the life of the patient as a whole. Ms Mueller compared treatment to a four-legged chair where all legs are needed to keep the chair from collapsing, i.e. medication, psychotherapy, psycho-education and self-help groups. Treatment should focus on recovery, as merely reducing symptoms is not enough; it should enable patients to lead a full and meaningful life, including being able to take up all one's social roles again and to work. The emphasis should be on the possibilities of the patient rather than on the limitations. Empowering patients and support their engagement with self-help groups and patient organisations will be a powerful ingredient towards recovery: self-help groups offer simple and low-cost peer support and offer psycho-education that helps patients to understand their symptoms better and communicate about them in a proactive way with their doctors.

Moreover, the volunteers active in the self-help groups or patient groups are positive and hopeful examples for other patients and the groups can motivate patients to follow through with their treatment and keep on taking their medication.

The groups also advocate for patients' rights and can serve as a useful contact point for professionals and researchers (on medication, expectations, use of apps etc). Professionals should not underestimate the expertise and knowledge present in patient groups.

Panel response

The first speaker was **Paul Arteel (GAMIAN-Europe),** who underlined the sad fact that some 50 % of all people diagnosed with a mental health problem do not receive treatment at all, due to geographical, financial and – most importantly - stigma thresholds. This is why combating stigma is at the top of the priority listings of all mental health patient organisations. The current EU Joint Action on Mental Health has recognised the importance of stigma and has put this topic as a cross-cutting theme in all of its work packages.

Treatment needs to be improved; it needs to lead to positive outcomes. However, what constitutes a positive outcome will be different for the different parties involved: it is not so easy to define. For hospital managers 'positive outcomes' will relate to lower cost, for patients it will mean a better quality of life, for psychiatrists reduction of symptoms are a consideration. This is why consensus is important in considering all those issues in discussions on outcome; all these perspectives need to be taken into account.
A survey carried out by GAMIAN-Europe 2 years ago found that ability to return to work is viewed by patients as the most important positive outcome.

Psycho-education is very important and often underestimated; it works in bipolar as well as in schizophrenic patients. In addition, the positive impact of peer-to-peer contact – as already underlined by Rebecca Mueller, has to be taken into account. More research is required to provide the 'hard' evidence that this is the case; examples of good practice already exist, but the effects of peer-to-peer contact should be measured properly.

Patients and their organisations need to have a stronger involvement in research on medicines and treatment – but in many cases, bureaucratic requirements and financial constraints exclude patients from doing so. If true involvement is required, the conditions for doing so need to be put in place.
Lastly, Mr Arteel underlined the potential of treatment via the Internet and eHealth applications.

The second panellist was **Marc Hermans (UEMS Section of Psychiatry),** who stated that, to date, research into drugs until now has focused on targeting intracellular processes. However, there is a high level of similarity in intracellular steering processes and a high risk of affecting other systems than the targeted ones (leading to undesirable side effects). One could therefore ask the question if the limits of the actual research possibilities paradigm of drug research have been reached. It could be argued that the pharma companies who give up CNS drug research are the most inspired ones. Is it time for a paradigm shift? Are drugs for brain disorders ready for retirement? If we do know too little about brain functioning in general, maybe we should prioritise research on brain functioning as such and temporarily refrain from research on drugs for brain disorders. After all, diagnosis is not important for the patients, but rather, for the health professionals. Patients are more interested in the prognosis. Maybe we should not conceive psychiatric nosology differently, but rather, develop a classification system based upon a list of mental functions. Knowing more about mental functions might allow for separate measurement of these functions, broadly picture a clinical image and focus research on specific mental functions. Making reference to Bayesian techniques seems adequate.

In relation to the White Paper, Mr Hermans underlined that it markedly neglects the possible input from practitioners; and it is precisely this input that is useful in developing databases collecting observational data. Large-scale databases collecting observational data allow for research on other causal factors and other therapeutic factors and clinical domains. While research on brain functioning and psychotherapy has low commercial value, it does have life-long added value. It would be interesting to take a critical look at the mechanisms and individuals involved in advising on research grants in this respect.
Lastly, Mr Hermans emphasized the importance of primary prevention, stating that global health has actually only poorly improved as a result of medical interventions – better hygienic measures have contributed far more.

Discussion

In the discussion the following issues were raised:

The need for a paradigm shift:
Some participants remarked that there is indeed the need for a paradigm shift as the area of mental health has not seen much improvement over the past decades. Psychiatry has dominated developments with policies being defined by psychiatrists. Alternative and more holistic treatments are not as highly valued – as can be seen from the fact that these are not reimbursed by insurance companies. The brain is a complicated organ; there is still very little knowledge about its true functioning. For instance, lithium seems to have a positive effect on bipolar disorder and has been prescribed for over 60 years – but what effect it has and why it works and what happens in the brain is not really known. There should be a more holistic and joint vision of what constitutes good treatment which includes the input of psychiatrists, psychologists, nurses, patients and families. Stabilisation of symptoms as the sole aim is not enough. While it is true that change has been slow, there has been change and this needs to be acknowledged. Collaboration between the various stakeholders is increasing. Areas where this paradigm shift can be seen:

- Increasingly better understanding between specialists and patients;
- decreasing patronising attitudes;
- Patients have become vocal and involved with their own healthcare;
- The social media have helped to better self diagnose and involvement with one's condition;
- There has been huge progress in bioscience area and brain imaging;
- Drug development has developed and has made a contribution to changing the lives of the patients.

However, the fact remains that more interdisciplinary collaboration between patients, doctors and other stakeholders is indeed still required. A paradigm shift can be effectuated more quickly if efforts of all stakeholders are united. Cooperation is the key word.

Need for more noise and better awareness:
Mental health remains at the bottom of the priority lists of policy makers, despite the clear impact on overall policy goals relating to the economy and employment. The sector needs to become more vocal.

Desired treatment outcomes:
What should be considered desired treatment outcomes needs to be redefined, taking patients' and their families' views into consideration; concrete 'outcome markers' would need to be developed. For instance, actions and treatment enabling patients to stay in or be able to return to work would be good markers. There are many possibilities to develop joint projects where patients and professionals could work together.

Need for biomarkers and large datasets:
Biomarkers are important and large databases are needed to determine what the most valid, reliable and useful biomarkers are in the field of brain and pharmacology research. It would be interesting to explore how industry can help to develop to these databases.

Health economic evidence:
The work done by the EBC on health economics is important as health economic evidence and health demographics can spur policymakers into action.

E-health, datasets and data protection:
E-health is an important factor and has enormous potential to contribute to access to mental health interventions.
The White Paper has not addressed the fact that health data should not be separated from the other kinds of data that we need in order to develop holistic treatment options and best management of mental illness. We need access to complete and comprehensive datasets, not only for the development of good healthcare provision but also for research.

However, there are issues relating to (health) data protection in the area of eHealth, also in terms of cross-border cooperation healthcare cooperation and compatibility of systems. It will be difficult to ensure complete and global data packages. We need to develop consensus and a common voice on what it is we actually want. It is way too early to strive for a global repository of data.

The importance of primary prevention in the field of mental health:
While primary prevention is usually related to physical illness, it is also vital in the area of mental illness. Health literacy is a must in this area and ways in which the pharma industry could be a partner in this need to be explored.

The need to include families as a stakeholder:
It is good to note that families are increasingly listened to and considered a vital partner in the treatment of those affected by mental illness. Families are in the first line and have the knowledge of patients that nobody else has. They are an indispensable part of patients' support systems and in many cases, stigma also extends to the family of patients.

Side effects:
In terms of research, the focus of drug research should also be on diminishing side effects.

Patients as experts by experience and supporters:
As patients have much to offer in terms of support to other patients, they are a valuable partner. They act as volunteers and need support as well. The expertise of patients is often undervalued and needs to be – formally- valorised.

The need for human contact in treatment:
There needs to be quality control of websites so that those who use them can rely on the quality and safety of the information. There are so many health apps – and while useful, it needs to be borne in mind that there has to be a person and the possibility of real contact behind it. Contact with patients is vital and should come first. Communication and life exchanges work best. Peer to peer interaction, the human connection is the most important and we should not have to prove by means of research that this is vital for the recovery and prevention of relapse. The mind and the brain are related but different entities and human connections can have an impact on brain itself.

Combating stigma:
Stigma related to mental health stems from lack of awareness. Those who don't know contribute to stigma. The experience of patients should be brought to wider audiences.

Defining the role of patients in patient-centred approaches and research:
Patient should be present in the discussions on research that concerns them, to ensure that the issues that matter to patients are taken into account. The patient perspective is indispensable.
The need for patient centred research on treatment and diagnosis is a recurring theme. Several projects exist in this area and these should be brought together. The White Paper should clearly describe the role of patients in this respect, and the patient role in treatment and diagnosis should be formally integrated into health systems and health budgets. The roles and responsibilities of the patients should be clearly defined. However, we need more scientific proof of the importance of the patient role, in order to convince policy makers to put these structures in place.

True patient involvement rather than tokenism:
If patients are going to be involved – for instance in outcome definition and clinical trials - it should be a matter of real involvement rather than tokenism. Actual structures must be put in place to facilitate this and resources will have to be found and set aside.

Christine Marking, 3 June 2015