Perspectives of Information-based Methods in Medicine: An Outlook for Mental Health Care

Jan Kalina[1] and Jana Zvárová[1,2]
[1]*Institute of Computer Science CAS, Prague, Czech Republic*
[2]*First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic*

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Abstract: Information-based medicine represents a concept characterizing the future ideal of medical practice overcoming the limitations of the popular concept of evidence-based medicine. The potential of information-based medicine is catalyzed by recent development of new technologies and basic research allowing to acquire a new medical knowledge relevant for an individual patient. The paper is focused on the specialty field of psychiatry. We discuss the challenges for the development of information-based psychiatry from the point of view of medical informatics together with its specific barriers and constraints. We discuss the development of telemedicine tools for psychiatric care, so far making mainly a disappointing experience. Medical informatics will also play the role in making results of basic research available to the psychiatrist at the point of care. Research results e.g. in molecular genetics or cognitive neuroscience will require to collect and analyze massive data on an individual patient. If these data are properly combined from various sources and analyzed, they represent an enormous potential for bringing a new psychiatric knowledge closer to an individual patient. This may contribute to improving the availability of psychiatric care and bringing its desirable destigmatization and humanization.

1 INTRODUCTION

The concept of evidence-based medicine (EBM) is widely accepted as a unifying idea describing the ideal practice of medicine. In our opinion, current clinical practice is gradually undergoing improvements towards more advanced ideals described by the concept of information-based medicine. This vision of future medicine emerges from the currently popular concept of evidence-based medicine and goes far beyond it.

The original concept of evidence-based medicine (Guyatt et al., 1992) is currently understood as a thorough, unique, and critical use of the best and most topical proofs in the process of decision making about the diagnosis, therapy, and prognosis for individual patients. The practice of evidence-based medicine integrates the individual clinical expertise of physicians with the best objective proofs coming from a systematically performed research (Sackett et al., 1996). It includes searching and systematic critical evaluation of publications with results of clinical research, analysis of activities, risk analysis, economic analysis of costs, or analysis of ethical and legal consequences of using a given approach (Eddy, 1990). Principles of evidence-based medicine also requires physicians to demonstrate their capability to use the newest research results and exploit them in their everyday clinical practice.

Within the framework of evidence-based medicine, it is the clinical evidence (i.e. acquired by clinical research) which is understood as the main source of clinical knowledge. Clinical trials remain to be the main source of clinical knowledge. However, they have serious disadvantages, e.g. artificial conditions or averaged results obtained by statistical methods for an averaged (virtual) patient, without taking his/her individual situation into account (Eddy, 1990). Further, properly designed clinical trials with small sample sizes have been argued to be suitable by proponents of personalized health care (Evans and Ildstad, 2001), i.e. focused on small groups of specific patients. In reality, there is however a tendency for clinical trials to be bigger and more expensive.

Current clinical practice is constantly enriched by quickly emerging new results of basic research. Thus, the clinical practice converges to an ideal state which we characterize by the concept of information-based medicine (Borangíu and Purcarea, 2008). This future

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ideal of medicine, although difficult be clearly defined and lying still far ahead, represents a new perspective paradigm in medicine, going beyond the current concept of EBM (Guyatt et al., 1992; Sackett et al., 1996) and overcoming its limitations. The concept describes the effort to transform the evidence for the (imaginary) averaged patient towards a real individual patient based on his/her individual data with clinical as well genetic or metabolic parameters measured by new technology. It requires to extract information from massive data sets.

This paper has the following structure. Section 2 presents our expectations that the information-based medicine will develop also in the area of psychiatry. Further sections discuss the role of medical informatics in the development of information-based medicine in the psychiatric field, which we call information-based psychiatry. We discuss its potential and benefits but also unrealistic expectations or specific barriers slowing down or complicating the development of information-based psychiatry. Telemedicine as one of e-health tools contributing to the development of information-based psychiatry is discussed in Section 3. Moreover, expected fundamental results of the basic research in molecular genetics or cognitive neuroscience will contribute to the development of information-based psychiatry as well, as discussed in Sections 4 and 5. Finally, Section 6 concludes the paper.

2 INFORMATION-BASED PSYCHIATRY

This section is devoted to the specialty field of psychiatry and uncovers sources leading to the development of information-based psychiatry.

Constantly, we can witness a gradual transform of psychiatry, which is enabled by a vast number of technological tools recently introduced for psychiatric care, including telemedicine applications such as decision support systems (Thornton, 2013). Information-based psychiatry will have to exploit available theoretical knowledge acquired in these tasks of basic (fundamental) research and to draw conclusions from measurements acquired for an individual patient, bringing the possibility of efficient therapy of psychiatric diseases.

Still, only a few results of the basic research (e.g. in neuroscience or molecular genetics) strongly contribute to bringing new sources of medical knowledge closer to an individual patient (Hanson and Levin, 2013; Lech et al., 2014). While intensive attention is paid to the research of genetic or neurophysiological causes of diseases and mechanisms leading to their development, the causes of some common psychiatric diseases remain to be unknown. For example, various sorts of psychosis are known to be caused by biochemical malfunctions of neurotransmitters in the brain, but the exact causes themselves have not been discovered yet. To give another example, Alzheimer disease cannot be currently cured due to the unknown cause. Other diseases are cured with sedatives bringing apathy and somnolence, but not removing the cause of the mental disease.

Currently, important sources of data or psychiatric knowledge (together with particular examples) include the following ones.

- Data measured by e-health tools for patient monitoring (e.g. non-stop wearable sensors);
- Signals (e.g. analysis of EEG or detection of depression due to voice changes in a speech record (Chen et al., 2005));
- Functional magnetic resonance imaging (fMRI) or other brain images (e.g. study of irreversible physical changes in the brain due to Alzheimer's disease or diagnosis of schizophrenia from a facial image (Dentico et al., 2014));
- Text in natural language (e.g. automatic analysis of unstructured medical reports in the electronic health record or analysis of computerized databases);
- Molecular genetic data (e.g. genetic predisposition to bipolar disorder or mood disorders);
- Voice analysis (e.g. detection of schizophrenia relapse in smartphones applications);
- Social network analysis (e.g. diagnosis of a depression relapse or automatic mood detection of facebook users;
- Biochemical or biophysical models of the brain exploiting differential equations;
- Time series (e.g. pharmacokinetical model for ethanol in the brain of an alcoholic);
- Connection between genes and fMRI brain images (e.g. genes responsible for the genetic disposition for schizophrenia (Liu et al., 2009)).

The fast improvement of technology and rise of big data of various types and formats from unthinkable sources have a potential to contribute to clinical usage and thus to a transform of psychiatry. Improvements in the effectiveness of therapy and patient safety are expected exploiting new knowledge obtained from a patient's data. This may allow to bring the process of decision making closer to an individual patient and also to make the therapy efficient, compared to the current state when the therapy of common diseases aims only at easing the suffering of patients. For all these reasons, the paradigm of evidence-based psychiatry should be replaced by deeper ideas going

beyond the vision of evidence-based psychiatry. In any case, the information within information-based psychiatry should be handled in a holistic approach (Zvárová, 2014), combining also economic and environmental aspects of data, information and knowledge.

3 TELEMEDICINE

Numerous telemedicine tools are currently being developed for psychiatry, exploiting modern e-health technologies for distant diagnosis, therapy and prognosis. Telepsychiatry enables to offer the psychiatric care also to patients with substance abuse problems, who would otherwise dare to search for a classical therapy. Telepsychiatric or telemental health services become popular in the United States, where they contribute to transforming the psychiatric care (Deslich et al., 2013) and help to increase access to mental health care. Telemedicine tools have the potential to be used in intensive attention as well as psychiatric assessment. They include videoconsultations between a psychiatrist and patient or mobile apps for smartphones. The aim of this section is to describe the beneficial impact and drawbacks of decision support systems in psychiatry.

Decision support systems (DSS) as telemedicine tools with the aim to offer assistance with clinical decision-making processes are generally believed to have a strong potential to improve health care across all clinical fields. Because a correct and effective use of the information has become the basis for the clinical decision making, they contain a statistical component combining information from different information components and comparing the risk corresponding to different alternatives (van Bemmel et al., 1996; Zvárová et al., 2009).

General advantages of decision support systems in various clinical fields can be summarized as follows.

- Potential for improving the quality of provided care and for generating economic benefits by reducing financial costs and saving human resources (Kalina and Zvárová, 2013),
- More comfort for the physician, a reduction of stress and more time for the patient,
- The possibility to exploit the level of knowledge according to the latest research developments in medicine,
- Useful assistance for a less experienced physician in a complicated medical case,
- Reduction of the patient risk by reducing the medication-related errors, reminding the physician not to omit important diagnostic examinations, warning about side effects or informing the physician about recent clinical knowledge.

In psychiatry, however, decision support systems have not become extensively used tools. Various attempts for decision support systems for the diagnosis (Bergman and Fors, 2008) and rarely for therapy (Trivedi et al., 2009) have lead to frustrations. Sometimes, it is claimed that the limitations of decision support systems rest in the technology but not in the medicine (Deslich et al., 2013). However, we claim that there are also limitations intrinsic in the substance of psychiatry, e.g. due to controversy in classifying psychiatric diseases (Thornton, 2013), vague psychiatric guidelines, or heterogeneity of symptoms and signs.

4 MOLECULAR GENETICS

Numerous psychiatric disorders including bipolar disorder or schizophrenia are largely affected by heredity. The genetic disposition represents a hidden potential, but it is now evident that there will be a long way to investigate the hereditary effect on the diseases and to use the research results to develop a personalized treatment. The molecular genetic research itself appears to be only at the beginning of investigating the genetic causes of common psychiatric diseases. The aim of this section is to discuss the limitations of the currently performed molecular genetic studies in the psychiatry domain and the role of medical informatics in bridging the gap between molecular genetics and clinical psychiatry.

So far, the benefit of currently available genetic examinations is very limited, which has been repeatedly denoted as frustrating and disappointing (Lohoff, 2010). Psychiatric genetics aiming at using molecular genetic knowledge in psychiatric care performed no significant progress and the heredity remained to a large extent unexplained. Only few genes suspect for being connected to psychiatric disorders have been identified, but still the discriminative accuracy of these genes is unlikely to be helpful for clinical utility, although the genes may formally yield statistically significant results (Pirooznia et al., 2012).

The genetic research has not met the enthusiastic anticipations of psychiatrists yet. We divide the reasons to two groups, common for the whole medicine and specific for psychiatry.

- General limitations of molecular genetics studies
  - General limitations of the technology of gene expression studies, genome-wide association studies (sequencing the DNA) (Daber et al.,

2013) or enrichment analysis searching for explaining the biological meaning of a group of genes (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014).
  - Insufficient validation of the results (Hasman et al., 2011); this is probably the main problem and the core of the so-called crisis of genomic medicine (Marshall, 2011).
  - Too expensive measurements (even nowadays).
  - Too big data to be analyzed reliably by currently available data mining methods (Kalina, 2014).
- Criticism of recent studies in psychiatry
  - Current studies were overly simplistic (Pirooznia et al., 2012).
  - Current studies do not take complex biological processes such as metabolic pathways into account. Such processes are however distributed across an entire network of genes being only subtle at the level of individual genes (Subramanian and Simon, 2010).
  - Even if the effects of several gene loci were cumulated, the associations among genes may be more complex than a simple model for the cumulation.
  - Controversy of currently available predictive genetics in psychiatry. For example, a genetic test for bipolar disorder is offered by commercial companies which is criticized by numerous experts for not being sufficiently validated (Mitchell et al., 2010).
- Specific limitations of psychiatry
  - Commonly, there is no single genetic variant responsible for the disease (Lohoff, 2010), the genetic dispositions is highly polygenic, i.e. caused by a large number of genes with a small contribution to the total genetic risk (Ellegood et al., 2015).
  - Some gene variants are rare (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014), thus requiring very large genetic studies (Lohoff, 2010).
  - A predisposition may not necessarily lead to the development of the disease, but life style and environmental factors play their role.
  - The disease may actually develop as a mere consequence of being diagnosed.

5 COGNITIVE NEUROSCIENCES

Understanding the brain will be crucial for the development of information-based psychiatry. It is believed that many of the following research tasks may be solved by means of fMRI, which already now offers numerous available techniques to help physicians to diagnose and treat medical conditions of the brain. The role of medical informatics within this research is documented by the fact that it has been designated as one of six main platforms of the Europe-wide Human Brain Project. While some experts are critical to the possibility to understand the brain on a purely biological basis (Zahourek, 2008), available more holistic approaches can be characterized as rather alternative from the point of view of current cognitive neuroscience, which is involved in the following primary research aims:

- Searching for a suitable model for the human brain. Earlier models of the brain had a fixed point of view according to the organization of the central nervous system. Such models exploit the knowledge of specific functions of individual parts of the brain. Nowadays, dynamics models of the brain are found more appropriate, which are based on large-scale distributed and interactive networks (Duffau, 2011).
- Using fMRI to predict whether a depressed patient will respond to treatment.
- Using fMRI images as predictors of conversion to dementia (Whelan and Garavan, 2015).
- The reasons of biochemical malfunctions in the brain are not discovered and we cannot expect a single precursor for their explanation.
- An early diagnosis of schizophrenia based on fMRI of the brain, which is as a highly heritable disease of unknown cause (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014).
- Investigating principles of spontaneous brain activity and especially connection between pairs of brain parts in the resting state (i.e. resting-state brain networks). This hot topic in current neuroscience contains the open problems of understanding of the brain processes at various activities or searching for a method for an effective monitoring of the brain. It is believed that modifications of the resting-state brain networks are characteristic for schizophrenic patients.
- Robust alternatives to current methods for the analysis of fMRI images. Neuroimaging is known to be highly sensitive to outliers due to measurement errors and complicated structure of acquiring the images. Robust procedures resistant to the presence of noise in the images have been proposed based on M-estimation (Wager et al., 2005), while more robust alternatives to severely outlying measurements (Kalina, 2012) would be desirable.

6 CONCLUSIONS

This paper presents our view of the ideals of information-based medicine, far extending the current ideals of evidence-based medicine. We believe that the concept of information-based medicine has a potential to become a popular buzzword in the future. In general, information-based approaches have spread already beyond medicine, e.g. to the concept of information-based policy in political and human sciences (Prakash and Potoski, 2012), where they replace the concept evidence-based policy.

In psychiatry, just like as in other clinical fields, the concept of information-based medicine expresses the potential to use new sources of data and knowledge to improve the everyday health care. The past decades teach us that new knowledge becomes introduced to standard psychiatric care slower compared to other clinical fields. Still, new results of basic research together with e-health technologies have an enormous potential to improve the health care quality, patient safety as well as reduction of expenses. These new results together with new tools lead us to describing the vision of psychiatric care by the concept of the information-based psychiatry. This paper describes the role of medical informatics in the process of development of information-based psychiatry.

However, we must be aware of specific features of psychiatry which represent serious limitations, barriers or drawbacks for the smooth development of information-based psychiatry. This paper discusses such specific features of psychiatry. We also discuss the current state of the art of basic research in fields important for the transform of psychiatry towards the information-based psychiatry. Important tasks in the process of development of information-based psychiatry include utilizing big data for an individual patient and their combination with new knowledge acquired by basic research. Other irreplaceable tasks include computer applications on various levels from the lowest ones (data storage and integration) up to using advanced tools of multivariate statistics and data mining for analyzing big data.

All these aspects together with desirable organizational changes of the psychiatric care are necessary (but not sufficient) tools endorsing the realization of the ideals of the paradigm of information-based psychiatry. Its potential is to combine data available from various sources, to analyze them and to bring the results as a new psychiatric knowledge closer to the patient allowing an improved availability, destigmatization and humanization of psychiatric care for an individual patient.

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