RESEARCH IN PSYCHIATRY: ONGOING DEBATE AND EVOLVING PRIORITIES

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The current status of research in psychiatry is less gloomy than implied by some recent reviews and commentaries. If psychiatric research seems to lag somewhat behind compared to other medical disciplines, the main reason is that the complexity of mental disorders has no equal in medicine and requires an equally complex multidisciplinary effort. However, it is probably true that we need some reconsideration and rebalancing of the priorities of psychiatric research, and it is certainly true that the viewpoint of the various stakeholders involved in the field, and in particular of users, has to be taken into account in this respect.

The notion that psychiatric research is in a crisis or in a stalemate has recently become a sort of cliché. Several very visible reviews and commentaries have asserted: a) that the diagnoses used as inclusion criteria in psychiatric research are invalid (e.g., [1]); b) that psychiatric research, in particular biological psychiatric research, has not been able to "determine what causes schizophrenia, depressive disorder or anxiety diseases", despite many decades of efforts [2]; and c) that the research documentation of the impact of psychiatric treatments is questionable (e.g. [3]). This climate of disillusionment and skepticism has generated a revival of the ideological split within our profession between those who believe that mental disorders are brain diseases and that psychiatry, as a clinical neuroscience discipline, "needs to invest greater scientific effort into studies of the etiology and pathophysiology of these major brain disorders" [4], and those who maintain that biological research "has failed to deliver anything of value to clinical psychiatrists and is very unlikely to do so in the future" [5].

These two opposite positions are now being increasingly stretched to the extreme, with the claim on the one hand that "it is time to end the distinction between mental and neurological illnesses" and that "psychiatric disorders should be reclassified as disorders of the (central) nervous system" [6], and on the other that it is the "technological paradigm" which has failed, since the balance of evidence does not support the idea that "mental health problems are best grasped through a technical idiom" (i.e., through psychiatric diagnoses) and that "good mental health work can be characterized as a series of discrete interventions" (i.e., specific pharmacological or psychotherapeutic treatments) [7].

Needless to say, these extreme positions actually converge in reinforcing the public perception that psychiatry lacks a coherent theoretical basis and that the credibility of whatever psychiatric research produces is at least doubtful.

What should our position be, as individual professionals and as psychiatric organizations, in this debate? A first point which in my opinion needs to be made is that the gloomy picture that both parties are presenting of the current status of psychiatric research is incorrect and based on simplistic assumptions and expectations. What do they mean when they state that psychiatry has not been able to determine "what causes schizophrenia, depressive disorder or anxiety diseases"? Are these people aware that the nature of mental disorders "does not yield up to a reductionist, 'one cause' etiological model" and that "this clear picture – where all roads lead to one essentialist cause – is really an exception even in general medicine" [8]? Indeed, the etiology of the most prevalent diseases in Western countries (e.g., hypertension or asthma) is now conceptualized as complex and multidimensional. There will be

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certainly no more "spirochete-like discoveries" in psychiatry [9], while what is occurring and is going to occur is the gradual elucidation of a multiplicity of risk and protective factors, which exert small to moderate effects at different levels and interact with each other in complex ways.

Using this key, one can appreciate that psychiatric research has made significant advances in the past few decades. Within a project funded by the European Commission, whose acronym is ROAMER, aiming to build up a roadmap for mental health research in Europe [10], a group of scientists has been recently asked to identify the main advances in psychiatric research during the last ten years. Well, the top two advances in the list have been "the increased understanding of gene-environment interaction as well as epigenetic mechanisms in psychiatry" and "the acknowledgement of effects of early (prenatal, perinatal, postnatal) environmental exposure and the increased understanding of the trajectory of common mental disorder along the lifespan (from childhood through adolescence into adult life)". One can easily appreciate that this research is much more complex and sophisticated, and congruent to the complexity of mental disorders, than the research that many critics of psychiatry have probably in mind, i.e., the old-fashioned comparison between a sample of patients with a given psychiatric diagnosis and a sample of healthy controls, in the search of a statistically significant difference with respect to the mean values of a given (usually biological) variable.

It can be argued that much of the above-mentioned new research has been designed and conducted not only by psychiatrists but also by other mental health and non-mental health professionals, but this is both unavoidable and welcome. Complex research requires multidisciplinary efforts, and the psychiatric profession will have an increasingly or the decreasingly prominent role in that research in the years to come as a function of its ability to realize what is now the direction of progress.

One could also argue that, in these new studies, the impact of several environmental and genetic risk factors has been found to display a substantial non-specificity for a range of mental disorders. But this should be regarded as an important research finding in itself, whose emergence has not been obstructed by the use of our current diagnostic systems. These systems, in spite of their limitations, have important merits, including the fact that they allow researchers to understand each other when they talk about a given mental disorder and to compare their findings. The existence of these systems does not prevent the emergence of other, new patterns of classification of mental disorder, based on neurobiological or behavioural or other elements, and these alternative patterns can certainly be used, and several of them have already been used, as independent variables in psychiatric research.

So, the status of etiopathogenetic research in psychiatry is less bleak than the above-mentioned reviews and commentaries imply, and our current diagnostic systems have not been an insurmountable obstacle to the progress of that research.

Coming to psychiatric treatments, is the currently emerging skepticism about their scientific foundation really justified? Well, I think that a major contribution in this respect has been provided by a recent review of meta-analyses comparing the efficacy of psychiatric vs. general medicine medications [11]. This review found that, for instance, the efficacy of antipsychotic drugs in the acute treatment of schizophrenia, evaluated in terms of standardized mean difference from placebo, is comparable to that of anti-hypertensive drugs in the acute treatment of hypertension, and is five times greater than that of thrombolytic medication in the acute treatment of stroke. Even more strikingly, the efficacy of antipsychotics in the maintenance treatment of schizophrenia is almost six times greater than that of angiotensin-converting enzyme (ACE) inhibitors in the long-term treatment of hypertension. The efficacy of antidepressants in the maintenance treatment of major depressive disorder is six times higher than that of ACE inhibitors in the long-term treatment of chronic heart failure, and the maintenance treatment of bipolar disorder with lithium is no. 3 in terms of efficacy among all treatments considered, being more effective than the long-term treatment of diabetes with metformin or asthma with corticosteroids.

These are the hard data. One could argue that the effectiveness of psychiatric medications in ordinary practice is lower than their efficacy as emerging in controlled trials, due to the poor adherence of patients to medical prescriptions and of psychiatrists to treatment guidelines. However, this is to some extent true also for medications used by other medical specialties. Furthermore, it is certainly not only our responsibility if the social context in which psychotropic drugs are used is marked by so much ignorance and ideological prejudice, thus inducing many patients and families to believe that these medications do not work and consequently to stop treatment or not to follow the prescription appropriately, and leading several psychiatrists to believe that it is not so important for

them to learn to use these drugs appropriately, since they represent only a marginal ingredient of care.
One could also argue that several psychiatric medications have significant side effects, but, again, this is true for many efficacious compounds used in medicine, and treatment guidelines are now available to prevent and address those side effects. Again, it is not only our responsibility if the use of these guidelines in ordinary practice is often not considered or even actively ostracized.
It could be further argued that the evidence of the efficacy of psychotropic drugs may have been biased by the financial conflicts of interests of investigators. However, again, this may be true also for the drugs used by other medical specialties. Moreover, it would be hard to maintain that financial conflicts of interests have had a significant impact on the evidence concerning the efficacy of lithium, a medication which has no support by the industry and has been found to be no. 3 in terms of efficacy among all drugs considered in the above-mentioned review. It could also be added that the role of ideological conflicts of interests of reviewers and commentators in minimizing or distorting the evidence of the efficacy of psychotropic drugs has no equal in the field of medicine, and that the impact of these ideological conflicts of interests on the public perception of the efficacy of psychotropic drugs is being at least as substantial as that of financial conflicts of interests [12].
So, the gloomy picture of the status of psychiatric research depicted in some recent literature is not correct. However, it is probably true that we need some reconsideration and rebalancing of the priorities of psychiatric research, and it is certainly true that the viewpoint of the various stakeholders involved in the field, and in particular of users, has to be taken into account in this respect.
Indeed, it has been pointed out that, in the field of health care in general, research agendas should reflect the needs and values of the people who use and pay for services, and that this is unlikely to be achieved without directly involving some of these people in research planning [13]. This argument is particularly relevant in the mental health field, since different stakeholders involved in this field may have different views about the desirability of various outcomes, with clinicians “typically affording pride of place to symptom reduction”, while the primary interest of families “is in receiving information, support and services” and people with mental health problems “are most concerned with issues of choice and control and the importance of decent lives” [14].

Within the above-mentioned ROAMER project, we conducted a survey among various categories of stakeholders about the priorities for mental health research in Europe [15]. The survey was carried out with the national associations of psychiatrists, psychologists and other mental health professionals, the national organizations of users and carers, and the national organizations of psychiatric trainees of the 27 countries of the European Union. A very simple online questionnaire was used, asking the respondents to select the top five priorities for mental health research in Europe from a list of research areas, with the option to identify further areas if needed, and to rate the importance and the level of development in their country of each of those research areas.
Both associations of psychiatrists and organizations of users and carers identified research on the quality of mental health services as the top one priority. The other four top priorities were different for those two groups of respondents, with psychiatrists highlighting research on early detection and management of mental disorders, new medications for mental disorders, ways to increase access to available treatments, and prevention of mental disorders, whereas users and carers laid emphasis on research on new psychological interventions for mental disorders, stigma and discrimination, rehabilitation and social inclusion, and health and well-being of carers [15]. These results seem to support the recently expressed view that some rebalancing of psychiatric research may be needed in favor of health service, social and community studies [2].
A further activity within the ROAMER project has been a series of meetings of representatives of European organizations of the various categories of stakeholders, aiming to collect their recommendations about how to increase the quality and impact of mental health research in Europe.
In these meetings, the stakeholders first of all pointed out that we need more collaboration in mental health research (more formal networks, including as many countries as possible; more multidisciplinary studies, especially in emerging integrative areas such as social neurosciences; sharing of databases of large studies after they are completed). A second recommendation was to more systematically involve users, from the very beginning, when research is planned. There are in fact already several successful experiences of participatory research in Europe [16]. A third recommendation, very much in line with one of the advances highlighted by the above-mentioned group of scientists, has been to integrate research through

the lifespan, giving priority to longitudinal cohort studies. It has been also argued that the evaluation of treatments, especially in the areas of psychotherapies and psychosocial interventions, needs to be better standardized, and that further research is needed about the active components of those interventions. It has been further noticed that we need to better explore and highlight the economic and societal impact of mental health and well-being and to conduct more systematic research on vulnerable groups, such as unemployed people, migrants, those living in poverty and people with handicap.

All these recommendations are clearly of great utility, but several of them raise a further issue: should psychiatric research focus on proper mental disorders, or should it also address the wide range of mental health problems which increasingly come to the attention of mental health services in the community [17]? There are at present different views about this issue. Some commentators (e.g. [18]) have recently echoed the old complaint by F. Redlich [19] that "psychiatry abandoned the island of psychiatric disease and was thus engulfed in the boundless sea of human troubles". However, there are areas, such as research on the precursors and prodromes of mental disorders and on the psychiatric consequences of natural disasters or of the ongoing economic crisis, in which a deeper knowledge of the ordinary, physiological responses to major stressors and life-cycle transitions is clearly necessary.

Psychiatrists need to collaborate with other mental health professionals and other relevant stakeholders in the characterization of these ordinary responses as well as of those more serious responses to the above stressors and transitions which are likely to come to the attention of mental health services although not being proper mental disorders [17]. It is useful to point out, in this respect, that the complete denomination of the ICD is "International Classification of Diseases and Related Health Problems", obviously including also mental health problems, and that both the ICD and the DSM already include chapters on "other conditions which can be a focus of clinical attention", although those chapters are at the moment somewhat elusive and of doubtful clinical relevance.

This broader focus on mental health problems which are not proper mental disorders could guide the development of cost-effective interventions and community resources for these problems. Currently, in fact, there is on the one hand the risk of an inappropriate extension of interventions used for proper mental disorders to the new emerging conditions (for instance, use of antidepressants for the understandable psychological consequences of the ongoing economic crisis), and on the other the risk to reduce the intervention to practical advice also in cases in which a professional management is needed. This research could also contribute to a clearer definition of the limits of the scope of mental health services, especially in the presence of substantially reduced resources [17].

Further recommendations to improve the quality and impact of psychiatric research have been provided within the ROAMER project [10]. One set of recommendations focused on training for psychiatric research. It was observed that there are at present no European curricula in mental health research training, that high-class senior researchers are often disincentivized out of the research system and leave it for private practice or other sectors, so that there is a lack of mentors. Problems in recruiting young people in psychiatric research were also pointed out. Another set of comments was about the persisting underfunding of mental health research as compared to the magnitude of the social burden related to mental disorders. There is a need to highlight the economic and societal impact of mental health, and to speak to governments and international organizations with a common language ("ask three psychiatrists and you get four answers": this is a common complaint by politicians and administrators and an excuse for not investing in mental health research). It was also argued that there is often a split in psychiatry between research units and technical facilities (they are too "independent" from each other), and not enough collaboration and sharing of resources (including protocols and databases) among research units. The need to massively invest in e-health and m-health approaches was also highlighted, and this is going to be endorsed in a major European project.

The promises and limitations of the Research Domain Criteria project, launched by the National Institute of Mental Health (NIMH) in the US with the aim to generate a diagnostic system based upon neuroscience and behavioural science rather than descriptive phenomenology [20], were also discussed. This project is more likely to develop neurobiological measures which help in subtyping rather than in replacing current diagnostic entities, in order to improve prediction of outcome and treatment response [21]. So, RDoC supporters should refrain from a polemic confrontation with the DSM and the ICD (e.g. [1]) which is unwarranted, disruptive to the field and confusing to patients and families and to the public opinion.

Furthermore, the gap between RDoC constructs and

the clinical phenomena we observe in clinical practice remains wide, especially in some areas such as that of psychoses. I recently chaired a meeting with the participation of the NIMH and the World Health Organization leadership, in which possible ways by which we clinicians can contribute to reduce this gap were considered, including a redefinition and dissection of complex symptoms (e.g., delusions), the search for experiential as opposed to behavioral intermediate phenotypes (e.g., the primary pathological experiences underlying delusions in schizophrenia), the refinement of currently identified dimensions of some mental disorders, a more precise characterization of some broader dimensional groupings or spectra (e.g., internalizing/externalizing disorders) and a refinement of the staging recently proposed for some mental disorders. Developing cross-walks between the RDoC and the current diagnostic systems, in a climate of reciprocal respect, is an endeavour that can only enrich psychiatry and related disciplines [21].

In conclusion, the current status of research in psychiatry is less gloomy than implied by several recent reviews and commentaries. If this research seems to lag somewhat behind compared to other medical disciplines, the main reason is that the complexity of mental disorders has no equal in medicine and requires an equally complex multidisciplinary effort. It is to be hoped that the ongoing debate will lead to an intensification and a further articulation and qualitative improvement of this effort, rather than resulting in a widespread demotivation or a revival of outdated polarizations.

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