Rev Psiquiatr Salud Ment (Barc.). 2012;5(3):135–138

Revista de Psiquiatría y Salud Mental

www.elsevier.es/saludmental

EDITORIAL

Solutions for patients depend on whether we can bridge the divide between social and natural science research approaches in the area of mental health☆

Las soluciones para los pacientes dependen de que podamos salvar la distancia que separa los enfoques de investigación de ciencias sociales y ciencias naturales en el campo de la salud mental

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Introduction

Research aimed at understanding the basis of mental disorders has expanded exponentially in the last decades. While many interesting findings have been produced, there have been no major breakthroughs in treatment over the last 20 years,[1] and treatments that once were considered breakthroughs, later were shown effective only in particular subgroups[2] or not more effective than simpler non-specific interventions.[3,4] Despite extensive research involving genetic, immunological, hormonal, cognitive, neurophysiological and neuroradiological variables, no diagnostic test, biological or other, exists for any mental disorder.

Two approaches can be envisaged to overcome this state of affairs. The first can be characterised as ''focussed'', i.e. to select a specific natural science focus that, coupled with better resources, may result in progress.[1] The other approach may be dubbed ''synergistic'', i.e. to examine whether opportunities exist for progress by synergistically connecting previously isolated activities in the areas of social and natural sciences. Here, the synergistic approach is discussed in more detail.

Within-discipline versus cross-discipline collaboration

Mental health research in the last decades has been carried out at many levels and across many disciplines (e.g. neuroscience, psychiatry, psychology, epidemiology, social sciences, methodology and statistics). Although recently there has been a move towards more cross-discipline and cross-technology approaches, research in the different disciplines continues to be conducted from a within-discipline rather than a truly cross-discipline perspective. The goal of this article is to clarify, on the basis of some of the best-known developments and achievements, the state of the art of research on mental disorders, and analyse gaps suggesting possible synergy from cross-discipline approaches. In the ''*Grand Challenges on Global Mental Health*'' initiative,[5] it is stated that ''future breakthroughs are likely to depend on

☆ Please cite this article as: Van Os J. Las soluciones para los pacientes dependen de que podamos salvar la distancia que separa los enfoques de investigación de ciencias sociales y ciencias naturales en el campo de la salud mental. Rev Psiquiatr Salud Ment (Barc.). 2012;5:135–8.

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discoveries in genomics and neuroscience, in tandem with exploration of the role of sociocultural and environmental contexts'', suggesting that perspectives crossing the traditional borders of the natural and social sciences will be increasingly relied on. However, the *when*, *what* and particularly the *how* of such cross-discipline integration remain entirely unclear. This article will critically analyse some examples of the content, organisation, and achievements of the various areas of mental health research, with a view to analyse gaps, weaknesses and opportunities for cross-discipline research in such a way that the likelihood of progress impacting on treatment is increased.

The elephant in the room of biological psychiatry: The two languages of mental health research

The level at which the majority of symptoms of the disorders defined in DSM-IV and ICD-10 are expressed is ''mental'', i.e. accounts of experience that are not directly observable with the quantitative methods of translational neuroscience and biological psychiatry. The assumption that the way themind relates to neural function is similar to the way the body manifests somatic illness is simplistic and unproven. In other words, the way paresthaesia is associated with multiple sclerosis may not apply to the way low mood relates to alterations in neural function; that the scientific reducibility of one to the other is more complex for low mood than it is for multiple sclerosis is evident. Although many would take the position that brain activity is necessary for mental symptoms, it is also reasonable to take the position that the connotations and vocabulary used in non-observable mental descriptions and explanations are essential, and cannot be reduced to the terminology and lower-level explanations of natural science. Mental health research thus necessarily makes use of two languages, one ''physical'', in which all phenomena are reducible to natural science, in which it is possible to ''explain'' by enumerating causal laws, the other ''mental'', reflecting a perspective in which human experience, unlike molecular processes, displays intentionality, meaning and so on, that is not reducible to natural science laws. Natural and the social sciences therefore face a natural divide when invited to work within the same research paradigm.

The existence of two languages in mental health research is one of the reasons that a paucity remains in crosstalk between areas (broadly) distributed over the social and natural sciences, even though the application of scientific paradigms to mental health research, including those derived from neuroscience, psychiatry, epidemiology, social science, sociology, psychology and philosophy have expanded exponentially. In other words, research in mental health has expanded exponentially, however in widely different directions, showing signs of increasing fragmentation rather than integration. If natural science and social science are to join forces, this will have to be at the level of joint research endeavours in which the results are interpreted on the basis of a common language. Although an interdisciplinary approach is sometimes adapted, this may in fact simply repeat the fragmented approach if separate groups making sense of the data; integration has to ultimately be at the level of making sense of the data in an integrated way, using a common language.

Pointers to elements that may be used to construct a common language

There are some examples of ''natural'' cross-discipline research findings that clearly show the potential to evolve further towards the use of a common language.

1. Research in epidemiology and social sciences highlights powerful effects of the social environment on the onset and persistence of syndromes of mental ill-health, the existence of vulnerable subgroups, and possible cognitive, neural and behavioural mediation of environmental effects.
2. Research in psychology and psychiatry indicates that most mental disorders as defined in DSM and ICD represent quantitative deviation from health.
3. Research in basic population genetics highlights the importance of (epi)genetic variation in terms of short-term and long-term adaptation to the social environment.
4. Research in social neuroscience highlights the role of the brain in enabling man to navigate the social world and to build models of the way in which one's current context – which includes both the social environment and one's internal states and traits–impacts on how we attach meaning to social cues. There is increasing interest in the role of culture on these processes, for example how cultural variation may impact on social cognition.

Elements 1–4 indicate that genetic variation and neural processes form the biological roots of human sociality, resulting in the mutual constitution of cultures and selves; they also suggest that health and illness result from complex interactions between the physical, cultural, and social environments. Thus, a common theme emerges linking deviation from mental health, genetic variation and neural function, which can be formulated as: dynamic adaptation to the individual-level and wider social environment. Dynamic adaptation to the environment may constitute a point of entry towards a common language in mental health research, linking social and natural sciences. However, this perspective contrasts with the current practice of research in biological psychiatry, which typically involves comparisons between a group of severely ill patients constrained by DSM or ICD criteria of disorder, and healthy, or ''super-healthy'', controls on static measures of, for example, allelic frequency or cortical thickness. In other words, the role of genetic and neural variables in dynamic adaptation to the social world, including at the level of intentionality and meaning, is typically not taken into account. The model underlying research of mental illness that currently arguably is most dominant, is that of genetic variation impacting adversely on neural circuits giving rise to symptoms of mental disorder,[1] in which the impact of the environment on brain development and gene expression is not considered,[6] let alone how meaning, intentionality and emotion may be mediated by these processes.

Conclusion: Integrating social factors in natural science research

Given the above, it is not difficult to construct some practical examples on how to integrate social sciences approaches in mental health research focussing on (i) genetics, (ii) neuroimaging and (iii) animal models, using the perspective of dynamic adaptation to the environment.

1. What potentially links the different approaches in mental health research is the level at which social and cultural influences are studied, and how these might interact with each other. Social science research is of particular interest in the area of how the wider social environment may impact on risk for and resilience against mental disorders. Examples of such contextual variables are area social cohesion and trust, area social capital, area social integration, area ethnic density, area population density, area social divide, etc. Research has shown that these types of contextual variables are strongly associated with mental outcomes (risk and resilience), and interact with individual-level characteristics (e.g. individual-level ethnic group and area ethnic density). As there is a paucity in cross-discipline approaches, this type of research has yielded little in terms of causality, biological and psychological mediators and moderators, and developmental pathways. It is reasonable to assume that the impact of the wider social environment will be mediated by individual-level cognitive and biological factors and that it will be moderated by the same factors. It is clear that a rich potential exists for collaboration between social scientists on the one hand, and mental health and neuroscience researchers on the other.
2. Mental health research in areas other than the social sciences usually has its focus on individual-level exposures and experience, and is well suited to help identify individual-level mediators of influences in the wider social environment, and identify the mechanism (psychological and neural) of interaction between individual-level and contextual environmental influences that promote risk or resilience. Similarly, neuroscience can build on experimental animal models of interaction between contextual and individual-level disease aetiology in the laboratory and focus on identifying and manipulating the underlying biological mechanisms.
3. A developmental perspective is essential, providing an opportunity to align animal models of early (including fetal) environmental impact on subsequent risk or resilience, with experimental and observational approaches in human research. Relatively little is known about biological and psychological changes in relation to changes in the (wider) social environment during 'normal' development, particularly in terms of their parallels and interplay, and how these relate to resilience and mental ill-health. Similarly, very little is known about how gene expression and the 'normal' epigenome change over time in the human brain,[7,8] and how changes may relate to the (wider) social environment and the onset of mental ill-health. For social scientists, there is a particular interest for social dynamics in the period of childhood and adolescence, as children and adolescents share social characteristics not only with their parents at home, but also with their peers at school, while the pubertal period is known for substantial hormonal and neuromorphological changes in the brain. These different contextual levels provide a rich background for studying the interaction between individual-level and contextual level environmental influences, and mediation and moderation by cognitive and biological systems.
4. Behaviour can be captured in different animal species and thus may form a common vantage point/phenotype that is usable for cross-discipline and translational research efforts. Although work is carried out in this area, human and animal experiments are rarely carried out in tandem with cross-evaluation of results. In addition, animal behaviour itself depends very much on social context (e.g. group/laboratory housing versus natural housing), requiring the addition of social science components to research. Also, there is room for increased collaboration on the basis of, for example, novel ''reverse translational'' approaches[9,10] or novel ''mental'' animal research paradigms.[11]
5. While it may be attractive to align cross-species behavioural research paradigms, resulting in a multilevel perspective on underlying neural mechanisms, there is an additional need to co-align and co-evaluate this work with 'mental' paradigms, for example from experimental psychology. A good starting point to bring together research on behavioural, neural and cognitive mechanisms around a single paradigm is to study the impact of a certain environmental exposure (at the level of repeated within-person momentary micro-environment, the individual level, or the contextual level of the wider social environment) impacting on mental, behavioural, neural, cellular and molecular outcomes in a single observational or experimental ''social'' paradigm, taking into account moderation of environmental influence by genetic factors (Fig. 1). For example, childhood adversity and having a minority position in society are important social risk factors with powerful effects that can be described in terms of developmental mental, molecular, cellular, neural circuit, cognitive and behavioural effects, in

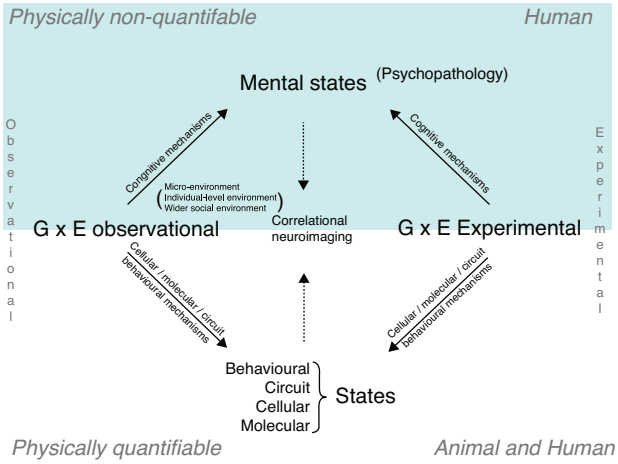

Figure 1 Bringing together research on molecular, cellular, neural circuit, cognitive and behavioural mechanisms from a single ''social'' research paradigm perspective.

association with evidence of moderation by genetic variation. Bringing these together in a single collaborative research effort, linking the different mechanisms, will make it possible to enrich the outcome of individual research efforts synergistically.

6. Finally, prevention and treatment are essential topics to consider in this context. As explained earlier, both ''mental'' and ''biological'' treatments that once were considered breakthroughs, later were shown effective only in particular subgroups[2] or not more effective than simpler non-specific interventions.[3,4] Integration of ''mental'' and ''biological'' approaches in mental health research can show cross links and point the way forward. For example, resilience against adversity is thought to be mediated by secure attachment, ability to generate positive emotions and having ''sense of purpose'' in life. A focus on the molecular mechanisms of these mental mediators may help strengthen these resilience factors. Similarly, experimental medicine approaches to jointly examine the mental and neural mechanisms of biological and non-biological treatments such as training or psychotherapy, may help devise treatments with more specific and/or more lasting impact.

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