Chapter 14: Neurobiological Models in Psychiatry

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"I want you to take note that in this machine all these functions follow naturally from the disposition of its organs alone, no more and no less than those of a clock or automaton follow from that of its counterweights and wheels"

Descartes (1662; 1998)

"Psychological Diseases are diseases of the brain…insanity itself is only a symptom"

Griesinger from Pathologie und Therapie der psychischen Krankheiten (1845) cited in Porter (1997)

"If mental disorders are brain disorders, then it follows logically that the basic sciences of psychiatry must include neuroscience and genomics"

Tom Insel (Insel and Quirion, 2005)

Introduction

The idea that psychiatric diseases are brain diseases has been a driving force in much of the conceptualisation of mental illness and its treatment. It has been held in counterpoise in the Western tradition by psychological or psychosocial conceptualisations of disease, the dominance of one particular conception ebbing and flowing. Advances in neuroscience have led to enthusiasm in the search for a neurobiological model of mental illness. However, no neurobiological model has been found that fully explains the syndromes treated by psychiatrists. And there is frustration at the lack of translation of new discoveries into effective treatments.

Neurobiological models of mental illness seek to understand psychiatric illness primarily or only in physical terms formed from the basic scientific knowledge around brain function: anatomy, genetics, proteomics, cellular mechanisms, neurotransmitters, physiology and connectivity. The models differ in their scale and ambitions from those that aim to describe a restricted or defined dysfunction (e.g., how might an auditory hallucination arise) as against a global model of brain function and disease. These models reference existing conceptualisations of how our brain works. These have tended to project the most complex technology of the day onto the problem of how the brain functions. In Descartes' era the metaphor of the watch in all its mechanical complexity was a compelling model of brain function (Draaisma, 2000). More recent iterations have built up models based upon the biophysical properties of neurons linked into a comprehensive computational model of the brain using electroencephalography and the underlying connectome of the brain (Shine et al., 2021). These models track the development of seizure activity convincingly but are less compelling when explaining mental illness.

In its most basic form, the biomedical model of disease, "assumes disease to be fully accounted for by deviations from the norm of measurable biological (somatic) variables" (Engel, 1977). Likewise, the symptoms and signs of disease can also be reduced to parts that can be analysed using the scientific method and be understood to be caused by a change in the functioning or anatomy of the body. Treatment of that change, by an expert such as a psychiatrist, should be able to fix the problem. Disease comes about in the individual, and the patient bears little responsibility for their disease but is expected to cooperate with treatment. In return, their illness is recognised and they have special rights to our care and compassion (Wade and Halligan, 2004). This simple model initially appeared to be of use in psychiatry with the identification of the effects of syphilis on the brain and the identification of the psychiatric and neurological manifestations of that disease. However, it has not coped well with the complexity of mental illness. It failed to take into account social, environmental and psychological factors, ignored prevention and presented illness as a neutral objective scientific process, which it most certainly is not. It has been caricatured as "mindless" psychiatry in opposition to the "brainless" modes of explanation that prioritise psychological models at the expense of any consideration of the body (Eisenberg, 1986).

The weakness of this casuistry can be seen from attempts to understand the aetiology of schizophrenia. The similarity of delusions and hallucinations to the effects of other illnesses or psychedelic drugs has suggested to many that this may be part of the explanation for positive psychotic phenomena in schizophrenia. The identification of an unusual catecholamine in the urine of people with schizophrenia, identified via a "pink spot" on urine chromatography (Friedhoff and Winkle, 1962), was initially thought to be similar to or a metabolite of mescaline and hence it was

proposed that schizophrenia was due to an inborn error of metabolism that caused the production of an endogenous psychomimetic substance. Further investigation of the metabolite found it to be related to the heavy tea consumption of institutionalised people and nothing related to the cause of their illness (Stabenau et al., 1970). Although this can be characterised as a naïve attempt to understand a complex illness, it also underlines the limitations of a reductionist neurobiological approach to test a hypothesis and find it wanting.

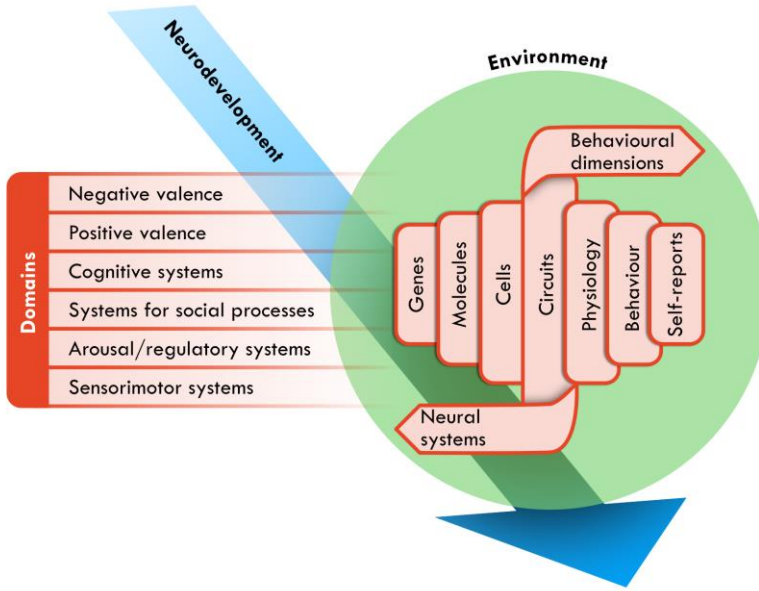

Figure 14.1. RDoC Framework for the understanding of mental illness (Cuthbert, 2020)

One of the hallmarks of the neurobiological models of disease is the expectation that function, and disorder will be identified through close examination of the constituent parts. These constituent parts are ultimately related to physical causes which invite physical interventions or treatments (Rocca and Anjum, 2020). A recent application of a neurobiological approach has been the Research Domain Criteria (RDoC) project (see Figure 14.1) (Insel et al., 2010). This considers cognitive and psychological dimensions as emergent properties of complex systems that become manifest as the system evolves and functions. These dimensions are not necessarily predictable on the basis of the bottom-up functioning of cells, and require a meeting of the bottom-up neurobiology with an understanding of top down hierarchical groupings that represent cognitive constructs (Insel et al., 2010). The RDoC model has eschewed conventional psychiatric diagnosis because of the lack of alignment of diagnoses with clear neuropathology, physiology or genetics.

However, it has not provided an alternate way of understanding health as against illness, or consider disability, all essential issues in describing illness. It may have reified measures which have as little scientific basis as the diagnoses they are replacing and mistake similarity in test performance for an underlying unity of causation – something which is unlikely (Weinberger et al., 2015). It also still under appreciates the significant effect of social forces in the development of illness (Marmot, 2015) and the bidirectional effect of psychosocial forces on the brain (Teicher et al., 2016). Finally, change on a test is not the same as illness. Without an understanding of disability caused, and the social context of the problem it causes, the change in the RDoC domain cannot be equated with the end effects known as disease and illness.

In addition to the difficulty that we are having understanding the complexity of the brain, all models of mental illness have to tussle with some basic issues around the characterisation of the disorders – equifinality, multifinality and multicausality (Cicchetti and Rogosch, 1996). Equifinality is the arrival at a common endpoint from many different causes. A significant depression can be seen as the outcome of loss, early life stress, influenced by social position, or as the sequalae of endocrine illness, brain lesions or genetic loading. Any single explanation of a mental illness may have validity for an individual and contribute to an understanding of the disease but cannot alone be equated with the disease. Current psychiatric practice would emphasise the complexity of causation and explain illness through the lens of multicausality, but leave it unclear as to how to proportion the many causes or how to measure them. Multifinality recognises that a single factor, such as early life stress, the effects of which can be measured biologically (Chu et al., 2019), or a gene that may have different effects depending upon the stage of development or the environment in which it is being expressed, can plausibly lead to a range of psychiatric illnesses, and that it is difficult to know which one will, if any, it result in. These factors, though seen in other complex systems are basic to the understanding of mental illness and make simple biomedical models unviable.

Neurobiological models of mental illness have provided important insights into the possible causes of mental illness but have not given rise to new treatments. Rather they have often been developed in response to the need to explain the effectiveness of those treatments, for example, the dopaminergic hypothesis of schizophrenia arose out of the observation that all effective antipsychotic medications were dopamine receptor blockers. Attempts to place mental illness onto a basic science platform, such as RDoC, although of heuristic value, have not shifted our understanding of nosology or treatment. Although individual diseases may be shelled out of the general syndromes that is treated by a breakthrough in understanding such as was seen with neurosyphilis, an understanding of the aetiology of the majority of mental illnesses has not yielded to a neurobiological explanation,

rather, understanding is best achieved through a synthesis of biological with psychosocial factors seen in a developmental context. This complexity makes psychiatry difficult, but this integration of psychosocial and developmental factors allows for a better conceptualisation of an illness in an individual and personalisation of their treatment plan.

Further Reading

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