Preface

In recent decades, biology and medicine have seen developments that differ uniquely from the research contexts of the past. If there is a single term that captures these developments and the new landscape that they shape, it is 'omics.' It represents an approach to describing a biological entity or system using detailed, multi-scaled, multi-dimensional data and equally complex analyses of the data, both made possible by bioinformatics. 'Omics' is synonymous with systems biology, which deals with the relational understanding of complex, collective systems of organisms. So widespread and intense have been the proliferation of omics disciplines that it has prompted the expression in jest, 'Who needs another omics discipline?'

To the brain-behavioral sciences, omics is a welcome and much needed approach. Unraveling the complexity of the brain and the intricacies of interactions between the genome, the brain, and the environment demands an approach commensurate in its sophistication. Powerfully emerging omics approaches applied to the brain are moving brain science into a new era. Numerous genetic loci are showing statistically significant associations with schizophrenia in genomic studies involving tens of thousands of cases. Brain circuits are being linked to gene modules via transcriptomic studies of brain tissue. Genome-to-phenome mapping has inspired the discipline of cognitive phenomics. Connectomics signals the prospect of dense and detailed mapping of neurons. And the US National Institutes of Mental Health has set in motion Research Domain Criteria (RDoC), an initiative toward a brain-based nosology of mental disorders where neural circuits and related phenotypic markers form the units of analysis.

These developments translate into various breakthrough achievements. Though remaining far from fully understood, it has long been recognized that a multitude of variables are orchestrated in brain development and in brain-behavioral relationships. Even a 'simpler' question such as the adaptation of a neural circuit to a new stimulus requires the study of numerous elements and variables. With the omics scale of data volume, data specification, data quantification, and complex mappings between multi-level data sets, the functionality and methods are provided to investigate complex questions such as follows: What might be the

polygenic nature of a mental disorder and how might this be expressed at subcellular and synaptic levels or at the levels of neural circuits? How do the permutations of multiple brain systems result in specific patterns in cognitive functional domains? and How can the spectral nature of many cognitive and psychiatric disorders be understood in terms of the differential expression of neural systems? Such questions, as this volume illustrates, are no longer lofty and solely theoretical. And they are beginning to compel major course changes in the clinical neurosciences. The development of RDoC is evidence enough of the near certainty that description and diagnosis of cognitive and psychiatric disorders will shift from categorical approaches to dimensional approaches—where discrete, separable cognitive, and neural features along various continua converge to form a diagnostic profile.

There are many ways by which psychiatry and neuropsychology can engage with this new research environment. This volume is about one all-important step. To both serve and benefit from a meaningful integration with the omics approach to the brain, cognitive and neural features need to be described in a standardized, scientific format. For the cognitive and neural phenome to be systematically linked to the genome and to other shaping or modulatory factors, and for this to be carried out in an omics/informatics environment, the units of analysis are critically important. They need to be precise and they need to have relational utility so that they can be tied to all their shaping mechanisms and developmental precedents. The term 'neurophenotype' is used in this volume as a general term to describe this kind of neural or cognitive feature. The neurophenotype approach to brain-behavioral associations and clinical diagnoses relies on precise cognitive and neural markers. It differs from approaches that are phenomenological-descriptive and detached from brain science (psychiatric diagnostic manuals), or approaches that compound many cognitive processes into a poorly operationalized amalgam (a subtest in a neuropsychological battery) and which, at best, can only be tied to the brain at a gross anatomical level. The neurophenotype approach facilitates the understanding of a profile of cognitive and neural features of an individual, the coexpression or variable expression of a common set of features across different diagnostic groups, and the biological mechanisms that may mediate the features.

The neurophenotype approach is, however, in its infancy. Neurophenotypes are currently not specified in a uniform or organized manner. Some of this has to with the difficulty of circumscribing processes or neural systems that may constitute neurophenotypes. If neuronal, circuit, or neuroanatomic phenotypes are viewed primarily in terms of genetic precedents, the possible impact of non-genetic factors can obviously be raised. If circuit neurophenotypes are viewed as central mediators of cognitive processes, then a host of intrinsic and extrinsic circuit modulatory variables complicate the picture, and the question of just what is the circuit, arises. There are many putative neurophenotypes. Many neural systems and cognitive processes have been cast into working definitions as neurophenotypes. All of these can be debated. Neurophenotypes and all their formalisms are evolving, but as a force. The current stage of this development and its associated topics, especially as applied to the clinical neurosciences, are discussed in this volume.

The volume was motivated by the authors' interests in cognitive neuroscience and neuroinformatics (Jagaroo) and cognitive and psychiatric genetics and bioinformatics (Santangelo). The vibrant intersections of neuroscience and genomics contextualized within a genome-to-phenome landscape can be felt throughout the research literature. It is hoped that capturing these developments and organizing the themes using the format of a composed volume will help better engage the clinical neurosciences in the discourse.

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