

Preface

No technological advance has had greater impact on our understanding of human brain function or our approach to understanding the underlying mechanisms of brain disease than the emergence of methods for the non-invasive imaging of the human brain. Over a period of three short decades we have moved from an almost complete dependence on animal models and post mortem analysis to an era in which the structure, function, and molecular composition of the brain may be reliably measured with increasing precision and resolution. This has led to a revolutionary approach to modern neuroscience whereby neuroimaging studies enable us to bridge from a cellular, molecular and systems level understanding derived from animal model systems all the way to human cognition, emotion and behavior. The chapters in this volume describe the major technical advances in non-invasive neuroimaging along with important clinical and translational applications in a range of human developmental states and diseases. The first several chapters focus on molecular imaging approaches using Positron Emission Tomography (PET), the second set of chapters focuses on using Magnetic Resonance Imaging (MRI) to reveal the structure, function, and molecular makeup of the brain.

Historically, PET research has focused on the brain dopaminergic systems, not least given the rich bounty of PET tracers targeting dopamine synthesis, plasma membrane transporters, and receptor binding sites. The first chapter by Volkow—a pioneering scientist in the use of PET to investigate dopamine transmission in addiction—gives a compelling insight into the brain mechanisms of this chronically relapsing brain affliction and the strong parallels of this disorder with obesity. This research has paved the way for neuroscientists interested in the causal attributes of dopamine dysfunction in psychopathology, specifically by aiding the development of translational models that capture key elements of clinical syndromes, including the addiction cycle. This has been no better exploited than the work of Gould and colleagues using a non-human primate model of stimulant addiction. Their review on neural vulnerability markers underlying addiction is thematic and timely to the concept of shared predispositions and clinical trajectories of several, often inter-related disorders such as addiction and attention

deficit hyperactivity disorder (ADHD), a point emphasized by Del Campo and colleagues where they discuss the neuroimaging correlates of ADHD and prospects for treatment.

While PET offers the ability to non-invasively assess alterations in receptor function, it does routinely require restraint of the animal in order to keep it stationary during the period of data acquisition. In pre-clinical research this is usually achieved by general anaesthesia and other supplementary devices to fix, for example, the head in one position. This approach places a serious impediment to correlating PET signals with behavior. A quantitative solution to this problem is discussed by Aarons and co-authors, which utilises the gold standard tracer [18F]-fluorodeoxyglucose. This is a must-read chapter for neuroscientists considering using this approach for their own experiments.

Other chapters highlight the importance of PET in the domain of neurological disorders, which by virtue of their progressive underlying molecular neuropathology are well-matched to powerful longitudinal studies to facilitate diagnosis and the development of new therapies. Huguchi and colleagues discuss this important and growing area of research by drawing on evidence from animal models of Alzheimer's disease (AD) and the targeting of biomarkers underlying the immune response to neurodegeneration.

Following this article Cumming and Borghammer provide a comprehensive synthesis of molecular imaging studies in Parkinson's disease (PD) that extend beyond dopaminergic biomarkers in the basal ganglia. The chapter highlights the extraordinary heterogeneity of PD in terms of motor and cognitive impairment as well as underlying neurochemical pathology.

Finally in this section, Praschak-Rieder and Willeit discuss the astonishing relationship between rhythmical seasonal variations (e.g. in light intensity) and monoamine markers in the brain. The authors focus on the serotonergic systems, and their own remarkable contribution to this field that have implications for understanding the neurobiology of seasonal affective disorder.

The second section of the book, focusing largely on MRI based measures, begins with an article by Hall, which reviews the exciting application of magnetic resonance spectroscopy (MRS) to profile metabolic abnormalities in neurological disorders such as AD and PD. A comprehensive review then follows by Maddock and Buonocore on the major metabolites and neurotransmitters that can be measured in the human brain using MRS, along with a discussion of the insights and controversies regarding the functional significance of these measures. It then reviews the spectroscopic findings in a broad range of psychiatric diseases including the anxiety disorders, major depression, bipolar disorder and schizophrenia. This exhaustive distillation of a very large and complex literature is a must read for experts and beginners alike pursuing spectroscopy in patients with mental disorder.

Functional MRI has become a very widely applied methodology for understanding the relationship between discrete functional neural circuits, cognitive and emotional processing and symptoms in psychiatric and neurological disease. One area that has been a proving ground for this methodology has been the

investigation of the neural basis of cognitive deficits in schizophrenia. Libby and Ragland review this literature and chart the evolution in thinking about the mechanisms underlying cognitive dysfunction in schizophrenia, which has paralleled our growing understanding of the cognitive and neural basis of higher cognitive functions such as attention and memory in basic cognitive neuroscience. They also emphasize the evolution of thinking from a lesion deficit model to a systems level analysis of cognition related brain activity.

Two chapters address important issues in the use of MRI to understand the ageing brain. Andreescu and Aizenstein review methodological issues related to conducting fMRI studies of cognition in ageing subjects, as well as findings related to functional changes of brain circuitry associated with late life mood disorders. Next, Carmichael and Lockhart describe the use of diffusion tensor imaging (DTI) to study white matter tracts in the human brain along with its application in understanding the important and potentially partly reversible contribution of white matter disease to cognitive ageing.

Salo and Fassbender review non-invasive neuroimaging studies of individuals with methamphetamine addiction, a major public health problem in the Western United States and many other areas of the world. These authors review MRI studies of brain structure and function and chemistry as well as a body of PET neurochemistry studies in this disorder. This work is discussed in the context of the known neurotoxic effect of methamphetamine as well as documenting the improvements in brain structure and function that are seen with abstinence from the drug.

In the final chapter Minzenberg provides a comprehensive review of the conceptual and methodological issues related to the use of pharmacological MRI in studies investigating the mechanisms of action of psychopharmacological treatments. This chapter also highlights the value of neuroimaging as a source of biomarkers, which may enhance clinical diagnosis and provide surrogate measures of treatment effects, an important advance for treatment development for brain disorders, which has lagged behind that for many other medical conditions.

The broad range of topics covered as well as the methodological depth provided throughout the volume will ensure that the reader is left with a strong appreciation for the progress that has been made in the development and application of brain imaging in behavioral neuroscience as well as the tremendous potential that exists for further major advances in the coming years.

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