Nutritional Neurosciences

Wael Mohamed
Firas Kobeissy *Editors*

Nutrition and Psychiatric Disorders

An Evidence-Based Approach to Understanding the Diet-Brain Connection

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Nutritional Neurosciences

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Editors

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I express heartfelt gratitude and deep appreciation as I dedicate this work to my wife, Dr. Rehab Ismaeil. Your unwavering support and unconditional love have been constant pillars throughout my academic journey and beyond. I am truly grateful for the love and inspiration you bring to my life, and I acknowledge that none of this would be possible without you.

Wael Mohamed
Kuantan, Pahang, Malaysia

To a special person I know, to Bassma Hajj-Ali, I dedicate this work.

Firas Kobeissy
Atlanta, GA, USA

Foreword

It was another usual busy day in the clinic, when my dear friend and colleague, Dr. El Hayek, approached me and asked if I could write the foreword for this book which focuses largely on the relationship between diet and mental health. For a moment, it felt like his invitation came as a wake-up call for me. For most of my colleagues working in mental healthcare, our day-to-day practice revolves around the traditional medical model of care, and though at the core of this is biopsychosocial approach to the care we strive to deliver, we don't seem to address the issue of diet or nutrition with the same rigour as we would for the likes of biochemical changes resulting from our prescribed medications. This area seems to attract a different, probably less superior regard, as compared to that for medication prescribing.

As we get along our clinical paths, and as we follow the approved guidelines that largely govern our clinical practice, we seem to lose touch with basics that underpin not only medical care, but also essential science that explains how the physiology, chemistry, and pathology of our bodies are all affected and governed by diet and nutrition. This is a branch of science related to the care of mental health which has been quite under-regarded so far.

You have in your hands a great compilation of the academic and professional experience and expertise of fellow colleagues from 14 different countries around the globe, in a worldwide collaboration to address diet and nutrition from different perspectives pertaining to mental health. The authors have scrutinised the body of evidence out there and have presented to the reader of this book robust evidence-based information upon which anyone interested in the ever-fascinating area of mental health, can find all necessary and up-to-date information on very interesting and topical-related topics. This book shall be a great source of information to guide many of us when considering advising our clients more professionally. It shall support our better understanding of this area and that interface.

I can't end my foreword without thanking Professor Kobeissy and Professor Mohamed enough for orchestrating the great work of that fine consortium of colleagues from around the world, to bring this valuable book to light, and a big thank you to all my fellow authors and co-authors. The impact of this work shall touch the

lives of many people. As the ancient Greek philosopher Pericles once said, “What you leave behind is not what is engraved in stone monuments, but what is woven into the lives of others”.

Erada Center for Treatment and Rehabilitation in Dubai Wael Foad
Dubai, United Arab Emirates

Preface

Exploring the intricacies of illness without books is like embarking on an uncertain voyage, while delving into books without the insights of patients is akin to remaining anchored to the shore.—Sir William Withey Gull (1816–1890)

Recently, the impact of nutrition and food intake has been highly investigated to study its impact on our brain function and development as it was shown that the diet we take will determine the outcome of certain brain disorders such as in brain injury and stroke. Along with its effects on cardiovascular diseases and cancer development, nutrition and diet have been shown to be involved in preserving our mental cognitive function and behavior. Recent studies have implicated that the development or exacerbation of certain neuropsychiatric disorders is related to an imbalance in our nutritional intake as observed in the development of obsessive-compulsive disorder (OCD), bipolar disorder, depression, and schizophrenia.

These findings have been driven by the revolutionary application of different "omics" fields and their application to studying the central nervous system (CNS) which broadened our understanding of fundamental neurobiological processes and has enabled the identification of proteins and pathways related to the complex molecular mechanisms underlying various diseases of the CNS. In fact, among these disciplines is the field of proteomics which has a subdiscipline of "Psychoproteomics" that evaluates the role of protein alterations in neuropsychiatric disorders aiming to identify biomarkers of such disorders. Furthermore, the fields of metabolomics and microbiome assessment have emerged to study the role of gut serotonin secretion and how it is implicated by "good" bacteria contributing to our sleep cycle, moods, and pain. Surveying the literature, we have noticed that there is a huge knowledge gap that discusses psychiatric health and the role of nutrition in modulating their outcomes. We are not implying that changes to our daily diet may be an alternative substitute for mental health intervention such as medication or psychoanalysis; however, we would like to highlight the role of a healthy diet and sound nutrition in alleviating certain psychiatric symptoms. Coming from a background of neuropsychiatric health research, the editors (Drs. Mohamed and Kobeissy) have decided to collaborate with other colleagues with expertise in the areas of psychiatric disorders and nutrition to address these knowledge gaps.

Overall, this new book provides updated and novel concepts in the field of psychiatry and its relation to food intake. The new compilation will be of high interest among researchers and clinical scientists involved in psychiatry, nutrition, and biochemistry.

Finally, we thank all the authors for their significant efforts in contributing such excellent chapters for this new edition. We are also sincerely grateful to each author for their patience during the compilation and final editing of this book.

Kuantan, Pahang, Malaysia — Wael Mohamed
Atlanta, GA, USA — Firas Kobeissy

Acknowledgments

First, we would like to express our great appreciation for all the authors who contributed to this timely project. The high level of devotion and dedication between the authors and editors made writing this book an enjoyable journey. In addition, we also extend our gratefulness to the authors who are in the fields of medical psychiatry and neuropsychiatric research for delivering years of their experience and work in different areas of psychiatric disorders to deliver such an elegant piece of work. The herein-discussed topics are of great value in the areas of nutrition, psychiatry, neurological disorders, and neurodegeneration. Finally, we would like to thank the encouragement of many of our friends and colleagues for their unconditional love, encouragement, and inspiration throughout the endeavor of the project.

Thank You

Wael Mohamed
Firas Kobeissy

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Wael Mohamed a Physician Neuroscientist, earned his Ph.D. from PSU, USA, and presently holds the position of Professor Madya at IIUM Medical School, Malaysia. With over 150 speaking engagements both domestically and internationally, Dr. Mohamed is a seasoned lecturer. He has authored more than 100 peer-reviewed papers in the field of Neuroscience/Psychiatry, boasting an h-index of 22. Additionally, he serves as an editor for several international Journals, having contributed to numerous journal special issues focusing on brain disorders. Furthermore, he is involved in editing several neuroscience books with several publishers. Dr. Mohamed has received research grants from esteemed national and international organizations including IBRO, ISN, MJF, STDF, FRGS, and INDO-ASEAN, totaling half a million US dollars in research funding. He is also the founder of the AfrAbia-PD-Genomic Consortium (AA-PD-GC).

Firas Kobeissy, PhD is a Professor of Neuroscience at the Department of Neurobiology, Neuroscience Institute Morehouse School of Medicine, Atlanta, GA, USA. Dr. Kobeissy serves as the Associate Director for the Center for Neurotrauma, Multiomics & Biomarkers (CNMB). Dr. Kobeissy obtained his Ph.D. from the University of Florida in the field of Neuroscience with a focus on brain injury biomarkers under the supervision of Drs. Ron Hayes and Kevin Wang. He obtained his Master's degree from the American University of Beirut, Beirut, Lebanon. His research spans utilizing different Multi-Omics applications related to brain injury models. Dr. Kobeissy has authored more than 300 articles, reviews, and book chapters along with two patents. He is the editor of nine books; these books involve brain injury, biomarker, and proteomics research. Dr. Kobeissy has served on several national and international grant review panels including the NSF, NIH, DoD, and the Department of Veteran Affairs. He served as the past president of the International Brain Research Organization—MENA chapter (2020–2023).

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Part I
Neurobiological Aspects of Psychiatric Disorders

Chapter 1
Neuroanatomy and Neuropathology of Psychiatry Disorders

Abayomi Oyeyemi Ajagbe, Michael Kunle Ajenikoko, and Abel Yashim Solomon

Abstract This comprehensive exploration delves into the intricate landscape of neuroanatomy and neuropathology in psychiatric disorders. The discussion synthesizes key findings from neuroimaging studies and research elucidating structural alterations in various mental illnesses, emphasizing the interplay between biological mechanisms, neuroplasticity, genetics, and environmental factors contributing to these changes. Integrating neuroanatomical insights into psychiatric diagnostics and treatment strategies offers promising avenues for precision medicine approaches, enabling targeted interventions tailored to individual neurobiological profiles. The significance of studying brain structure in advancing psychiatric care is underscored, highlighting the potential for innovative therapeutic interventions and the imperative need for ongoing research focusing on multimodal imaging, longitudinal assessments, and deeper investigations into the dynamic nature of neuroanatomical alterations. Emphasizing the clinical implications and future directions, this exploration underscores the pivotal role of understanding brain structure in shaping the landscape of mental health care, offering a foundation for improved patient outcomes and advancements in the field.

Keywords Neuroanatomy · Neuropathology · Psychiatric disorders · Neuroimaging · Neurostimulation

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1.1 Introduction to Neuroanatomy and Neuropathology in Psychiatry

Understanding the intricate relationship between neuroanatomy, neuropathology, and psychiatric disorders has become an imperative aspect in the field of mental health research (ENIGMA Bipolar Disorder Working Group et al. 2018; Goodkind et al. 2015). The convergence of neuroscience and psychiatry has unveiled remarkable insights into the structural underpinnings of various psychiatric conditions, shedding light on the neural substrates involved in mood regulation, cognition, and emotional processing (Decety and Moriguchi 2007; Malhi et al. 2015; Schumann et al. 2014).

Neuroanatomy, the study of the structure and organization of the nervous system, plays a pivotal role in delineating the neural basis of psychiatric illnesses (Blond et al. 2012; Vago et al. 2011). Concurrently, neuropathology investigates the structural and functional changes in the nervous system associated with disease states, offering critical insights into the pathological mechanisms underlying psychiatric disorders (Lucassen et al. 2014; Lyketsos et al. 2007).

Research conducted over recent decades has elucidated specific neuroanatomical alterations associated with diverse psychiatric conditions (Gong et al. 2019; Lui et al. 2016). For instance, studies employing advanced neuroimaging techniques have highlighted aberrations in key brain regions implicated in mood disorders, such as the prefrontal cortex, limbic system (including the amygdala and hippocampus), basal ganglia, and thalamus (ENIGMA Bipolar Disorder Working Group et al. 2018; Ng et al. 2009; Phillips and Swartz 2014). Such findings have not only contributed to unraveling the neural circuitry underlying these disorders but have also paved the way for novel diagnostic and therapeutic strategies.

The intricate interplay between genetic predisposition, environmental influences, and neurodevelopmental factors shapes the neuroanatomical architecture and contributes to the manifestation of psychiatric disorders (Akdeniz et al. 2014).

This chapter seeks to explore these multifaceted aspects, considering the pathophysiological mechanisms that underlie neuroanatomical changes observed in psychiatric conditions. Moreover, in the context of nutritional psychiatry, understanding the influence of diet and nutrients on brain structure and function is gaining prominence. Emerging evidence suggests a potential link between dietary patterns and neuroanatomical alterations in mental health disorders, emphasizing the significance of nutrition as a modifiable factor influencing brain health.

As we delve deeper into the neuroanatomy and neuropathology of psychiatric disorders, this chapter aims to synthesize existing knowledge while highlighting the gaps in understanding, thereby paving the way for future research directions in this evolving field.

Understanding brain structure is paramount in unraveling the complex underpinnings of mental health disorders. The brain's structural organization plays a fundamental role in shaping human behavior, cognition, emotions, and overall mental

well-being (Goodkind et al. 2015). Here are key points outlining the significance of comprehending brain structure concerning mental health:

Neural basis of mental health disorders: Brain structure forms the foundation for understanding the neural basis of mental health disorders (Schumann et al. 2014). Variations or alterations in specific brain regions, neural circuits, and connectivity patterns are often associated with various psychiatric conditions (Segal et al. 2023). For instance, structural changes in the prefrontal cortex, hippocampus, amygdala, and other regions have been linked to conditions like depression, anxiety, bipolar disorder, and schizophrenia.

Insights into cognitive and emotional functions: Different brain regions have specialized functions related to cognition, emotion regulation, memory, decision-making, and social interactions (Dehghani et al. 2023). Understanding how structural variations impact these functions helps elucidate the mechanisms underlying mental health disorders. For instance, changes in the amygdala's size or activity can affect emotional processing, potentially contributing to anxiety or mood disorders.

Advancements in neuroimaging techniques: Technological advancements in neuroimaging, such as magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), and positron emission tomography (PET) scans, have enabled researchers to visualize and analyze brain structure and function non-invasively (Annavarapu et al. 2019; Goodkind et al. 2015; Yen et al. 2023). These tools allow for the identification of structural abnormalities or differences in individuals with psychiatric disorders compared to healthy individuals, offering valuable insights into the neurobiology of mental illnesses.

Personalized medicine and treatment approaches: Understanding individual variations in brain structure could pave the way for personalized medicine in mental health (Bora and Pantelis 2015; Schumann et al. 2014). It can assist clinicians in tailoring treatments based on an individual's neuroanatomical profile, leading to more targeted interventions and better treatment outcomes.

Early detection and intervention: Detecting structural changes in the brain associated with mental health conditions may enable early identification and intervention (Jiang et al. 2022). Early intervention is crucial in preventing the progression of certain disorders or mitigating their impact on an individual's life.

Research and therapeutic development: Research focusing on brain structure in mental health provides a foundation for developing novel therapeutic approaches (Goodkind et al. 2015). Insights gained from studying neuroanatomy and neuropathology contribute to the development of new medications, therapies, and interventions that target specific brain regions or neural circuits affected by psychiatric disorders.

In summary, comprehending brain structure is a cornerstone in addressing the complexities of mental health disorders (Bora and Pantelis 2015). It offers a crucial framework for research, diagnosis, treatment, and the development of interventions aimed at improving the lives of individuals affected by psychiatric conditions.

1.2 Depression

Depression, a complex and debilitating mental health disorder, is intimately associated with alterations in brain structure and function (Zhang et al. 2018). Neuroimaging studies have revealed distinct neuroanatomical changes in individuals affected by depression, offering critical insights into the neural underpinnings of this condition (Zhang et al. 2018).

1.2.1 Neuroanatomical Alterations Associated with Depression

Depression is characterized by significant neuroanatomical alterations observable through various neuroimaging techniques (Goodkind et al. 2015). Studies utilizing MRI and other imaging modalities consistently indicate structural changes in specific brain areas among individuals with depression (Han and Ham 2021). These alterations include reductions in gray matter volume, disruptions in white matter integrity, and aberrant neural connectivity patterns that correspond to depressive symptoms (Grieve et al. 2013; Smagula and Aizenstein 2016).

Notably, reduced hippocampal volume and altered amygdala function are among the most extensively studied neuroanatomical changes in depression (Hamilton et al. 2008; Yao et al. 2020). The hippocampus, known for its role in memory and emotion regulation, often exhibits reduced volume in individuals experiencing depressive episodes (Malykhin et al. 2010; Videbech 2004). Concurrently, the amygdala, a key component of emotional processing, tends to show heightened activation and structural changes associated with altered emotional responses in depression (Arnone et al. 2012; Park et al. 2019).

1. *Prefrontal cortex*
   The prefrontal cortex, encompassing the dorsolateral prefrontal cortex (DLPFC) and ventromedial prefrontal cortex (VMPFC), exhibits structural and functional abnormalities in depression (Goodkind et al. 2015). Disruptions in these areas are linked to impaired executive functions, emotional regulation deficits, and altered decision-making commonly observed in individuals with depression.
2. *Limbic system (amygdala and hippocampus)*
   Dysregulation within the limbic system, including the amygdala and hippocampus, contributes significantly to the emotional disturbances characteristic of depression (He et al. 2020). Altered amygdala reactivity and decreased hippocampal volume are closely associated with heightened emotional responses, impaired memory, and altered stress processing in depressive states (Belleau et al. 2019; Roddy et al. 2021).
3. *Anterior cingulate cortex (ACC) and insula*
   Structural and functional changes in the anterior cingulate cortex (ACC) and insular cortex are observed in depression (Goodkind et al. 2015; Maywald et al.

2022). These alterations are linked to disruptions in emotional regulation, self-referential thinking, and altered perception of bodily sensations, contributing to the subjective experiences of depression (Maywald et al. 2022).

Understanding these neuroanatomical changes in depression provides a crucial framework for elucidating the neural basis of depressive symptoms (Schmaal et al. 2020). Such insights offer promising avenues for targeted interventions and treatment approaches aimed at modulating specific brain regions or neural circuits affected in depression. Integrating neuroanatomical research with clinical practice holds the potential for more precise diagnostic tools and personalized therapeutic strategies to alleviate the burden of depression on affected individuals.

1.3 Anxiety Disorders

Anxiety disorders, encompassing various conditions such as generalized anxiety disorder (GAD), panic disorder, social anxiety disorder, and others, are closely associated with distinctive neuropathological correlations and alterations in specific brain regions contributing to the manifestation of anxiety symptoms (Shin and Liberzon 2010).

1.3.1 Neuroanatomical Changes in Anxiety Disorder

1. *Amygdala*: The amygdala plays a pivotal role in processing emotions, particularly fear and threat detection (Adolphs 2008; Fossati 2012). Altered amygdala reactivity and connectivity are consistent findings across various anxiety disorders, contributing to heightened emotional responses and exaggerated fear perception (Forster et al. 2012).
2. *Prefrontal cortex*: Structural and functional abnormalities in the prefrontal cortex, including the dorsomedial prefrontal cortex (DMPFC) and anterior cingulate cortex (ACC), are implicated in anxiety disorders (Santos et al. 2019; Shin and Liberzon 2010). Disruptions in these regions affect emotional regulation, attentional control, and fear extinction processes, exacerbating anxiety symptoms.
3. *Insular cortex*: The insula is involved in interoception and emotional awareness (Gogolla 2017). Changes in the insular cortex are associated with altered bodily sensations and emotional processing, contributing to the somatic symptoms and heightened self-awareness seen in anxiety disorders (Gogolla 2017; Grossi et al. 2017; Strawn et al. 2015).

1.3.2 Neuropathological Correlations with Different Anxiety Disorders

1. *Generalized anxiety disorder (GAD)*: Neuroimaging studies indicate alterations in the amygdala, prefrontal cortex, and insula in individuals diagnosed with GAD (Madonna et al. 2019; Kolesar et al. 2019). These structural and functional changes are associated with heightened fear responses, emotional dysregulation, and exaggerated worry, core features of GAD.
2. *Panic disorder*: Distinct neural alterations in the amygdala, hippocampus, and brainstem regions have been observed in individuals with panic disorder (Shin and Liberzon 2010). Aberrations in these areas contribute to increased threat perception, altered fear conditioning, and dysfunction in the brain's fear circuitry, culminating in panic attacks.
3. *Social anxiety disorder (SAD)*: Structural changes in the amygdala, prefrontal cortex, and insular cortex are commonly reported in individuals with SAD. Dysregulation in these brain regions underlies heightened social threat perception, fear of negative evaluation, and difficulties in social interactions characteristic of SAD.

Understanding the neuropathological correlations and affected brain regions in anxiety disorders provides critical insights into the underlying neural mechanisms driving anxiety symptoms. These findings have implications for targeted interventions aimed at modulating specific neural circuits to alleviate the burden of anxiety and improve the effectiveness of therapeutic interventions.

1.4 Bipolar Disorder

Bipolar disorder is a complex mood disorder characterized by recurrent episodes of mania, hypomania, and depression, with significant neuroanatomical implications that underlie its symptomatology (ENIGMA Bipolar Disorder Working Group et al. 2018; Strakowski et al. 2012).

BD is also known as "manic depression" because it is marked by high emotional states that last days to weeks and include manic/hypomanic (abnormally elated or irritated) or depressed (sad) episodes (Franchini et al. 2022). BD frequently manifests and is diagnosed during adolescence, when there is a shift in the processing of emotion and cognition from earlier developing subcortical gray regions to increased use of prefrontal brain structures, a time when the brain may be especially vulnerable to developmental neuropathologies (Bi et al. 2022; Emsell and McDonald 2009; Lim et al. 2013).

1.4.1 Neuroanatomical Changes Observed in Bipolar Disorder

Neuroimaging studies have revealed substantial neuroanatomical alterations in individuals diagnosed with bipolar disorder (BD) (Emsell and McDonald 2009; Houenou et al. 2011). Structural neuroimaging findings consistently report volumetric alterations and disruptions in gray and white matter integrity, particularly in brain regions associated with emotional regulation and mood control (Gray et al. 2020; Strakowski et al. 2012).

1. *Prefrontal cortex*: The prefrontal cortex, including the dorsolateral prefrontal cortex (DLPFC) and ventromedial prefrontal cortex (VMPFC), exhibits structural abnormalities in individuals with BD (ENIGMA Bipolar Disorder Working Group et al. 2018; Guo et al. 2021). These alterations contribute to executive function deficits, emotional dysregulation, and impaired decision-making observed during mood episodes (Guo et al. 2021).
2. *Amygdala and hippocampus*: Studies indicate variations in amygdala and hippocampal volumes in BD, impacting emotional processing, memory, and stress responses (Blumberg et al. 2003; Cao et al. 2016). Dysregulation in these limbic structures is associated with emotional intensity and affective instability observed in bipolar disorder (Henry 2012; Nabulsi et al. 2020; Townsend and Altshuler 2012).

1.4.1.1 Impacted Brain Structures Contributing to Mood Disturbances

1. *Limbic system dysfunction*: The dysregulation within the limbic system, particularly involving the amygdala and hippocampus, contributes significantly to mood disturbances in bipolar disorder (Blond et al. 2012; ENIGMA Bipolar Disorder Working Group et al. 2018; Townsend and Altshuler 2012). Altered functioning and connectivity in these areas are linked to emotional dysregulation, increased reactivity to emotional stimuli, and the oscillation between manic and depressive states (Blond et al. 2012; Townsend and Altshuler 2012).
2. *Prefrontal cortical dysfunction*: Abnormalities in the prefrontal cortex, affecting emotion regulation and cognitive control, contribute to mood instability and the inability to modulate emotional responses characteristic of BD (Cao et al. 2016; Green et al. 2007; Sankar et al. 2021). Dysfunction in this region plays a crucial role in the transition between manic and depressive episodes (Wei et al. 2017).

1.4.2 The Neuropathology of BD

Bipolar disorder (BD) lacks the diagnostic neuropathology that characterizes and identifies the dementias, like other "functional" mental diseases, although this does not imply that BD lacks morphological correlations (Harrison et al. 2020). Studies

using magnetic resonance imaging (MRI) reveal subtle but significant variations in the sizes of various brain regions, including smaller hippocampus, amygdala, and thalamus, as well as thinner cortical layers (Harrison et al. 2020). White matter declines are also supported by more and more research (Harrison et al. 2020). Although results have been inconsistent, postmortem neuropathological examinations have been scarce, and few research have looked at at-risk people, or early-stage BD, or conducted longitudinal studies, imaging studies largely support the idea that BD has a neurodevelopmental genesis (O'Shea and McInnis 2016). Imaging studies and meta-analyses of them have consistently found the following abnormalities in the BD brain: ventricular enlargement males with BD had smaller corpus callosums, lower prefrontal white matter volumes, larger cerebellar vermis volumes, and smaller prefrontal cortical areas (O'Shea and McInnis 2016).

Bipolar disorder's neural basis involves intricate alterations in brain structures, particularly in the prefrontal cortex and limbic system, contributing to mood disturbances and fluctuating emotional states observed in affected individuals. Understanding these neuroanatomical changes offers insights into targeted interventions aimed at modulating specific brain regions to manage mood swings and improve the overall quality of life for individuals with bipolar disorder.

1.5 Schizophrenia

Schizophrenia is a severe and chronic mental disorder characterized by disruptions in thought processes, perceptions, emotions, and behavior. The neural basis of schizophrenia involves multifaceted neuropathological aspects and alterations in specific brain structures and neural pathways (Baldaçara et al. 2008; Howes and Kapur 2009; Van Erp et al. 2018).

1.5.1 Brain Structure Alterations and Neural Pathways Linked to Schizophrenia

1. *Prefrontal cortex dysfunction*: Structural and functional abnormalities in the prefrontal cortex, including the dorsolateral prefrontal cortex (DLPFC), are prominent in schizophrenia (Meyer-Lindenberg et al. 2005; Smucny et al. 2022; Van Erp et al. 2018). Disruptions in this region are associated with impaired executive functions, decision-making, and working memory deficits observed in individuals with schizophrenia.
2. *Hippocampus and limbic system*: Alterations in the hippocampus and limbic system are prevalent in schizophrenia, contributing to deficits in memory, emotional regulation, and disturbances in the integration of sensory information (Boyer et al. 2007; Harrisberger et al. 2016; Howes and Kapur 2009). These changes are

linked to the hallucinations and emotional dysregulation characteristic of the disorder.

1.5.2 Neuropathological Aspects Associated with Schizophrenia

Neuropathological studies of schizophrenia reveal a spectrum of abnormalities encompassing alterations in brain morphology, neurochemistry, and synaptic connectivity (Coyle et al. 2020; Van Erp et al. 2018). These include:

1. *Cortical abnormalities*: Studies consistently report alterations in cortical thickness, reduced gray matter volume, and disruptions in the parietal, temporal, and frontal cortices among individuals with schizophrenia (Schultz et al. 2010; Van Erp et al. 2018; Xiao et al. 2015). These structural changes contribute to cognitive deficits and disruptions in sensory processing observed in schizophrenia.
2. *Dysregulated neurotransmission*: Dysfunctions in neurotransmitter systems, particularly dopamine and glutamate, are implicated in the pathophysiology of schizophrenia (Goff and Coyle 2001; Howes and Kapur 2009; McCutcheon et al. 2020; Meisenzahl et al. 2007). Dysregulation of these neurotransmitters contributes to altered synaptic transmission, leading to cognitive impairments and positive and negative symptoms of the disorder (McCutcheon et al. 2020).

Understanding the neuropathological aspects and brain structure alterations associated with schizophrenia is crucial for unraveling the complexities of this disorder. Insights into the neural pathways linked to schizophrenia offer opportunities for the development of targeted interventions aimed at ameliorating cognitive deficits, managing symptoms, and improving functional outcomes for individuals affected by schizophrenia.

Several neuroanatomical features are shared among various psychiatric disorders, suggesting common underlying mechanisms:

1. *Prefrontal cortex alterations*: Studies indicate structural and functional abnormalities in the prefrontal cortex across multiple psychiatric illnesses, including depression, bipolar disorder, schizophrenia, and anxiety disorders (Goodkind et al. 2015; Hibar et al. 2018). Dysregulation in this region contributes to impairments in executive functions, emotion regulation, and cognitive control observed across these conditions.
2. *Limbic system involvement*: Aberrations in the limbic system, particularly the amygdala and hippocampus, are commonly implicated in mood disorders (depression and bipolar disorder), anxiety disorders, and schizophrenia (Van Erp et al. 2018). Altered emotional processing, memory disturbances, and stress response abnormalities are shared features associated with these conditions.

While there are shared neuroanatomical alterations, distinct neural patterns specific to each psychiatric disorder also exist:

1. *Dopaminergic system dysfunction in schizophrenia*: The dopamine hypothesis highlights the role of dopaminergic abnormalities, particularly in schizophrenia, contributing to positive symptoms such as hallucinations and delusions (Howes and Kapur 2009). This neural pattern is distinct and specific to schizophrenia.
2. *Glutamatergic dysregulation in mood disorders*: Studies emphasize the involvement of altered glutamatergic neurotransmission in mood disorders like depression and bipolar disorder (Maletic and Raison 2014; Yüksel and Öngür 2010). Dysfunctions in glutamate pathways contribute to mood disturbances and cognitive impairments unique to these conditions.

Certain brain regions and neural circuits exhibit overlap in their involvement across various psychiatric illnesses:

1. *Default mode network (DMN) dysfunction*: Disruptions in the DMN, including the medial prefrontal cortex and posterior cingulate cortex, are observed in depression, anxiety, and schizophrenia (Goodkind et al. 2015). Altered connectivity within the DMN is associated with impaired self-referential thinking and rumination, features seen across these conditions.
2. *Hypothalamic-pituitary-adrenal (HPA) axis dysregulation*: Abnormalities in the HPA axis, involved in stress response, are implicated in depression, anxiety, and some aspects of bipolar disorder (Jacobson 2014; Maletic and Raison 2014; Phillips et al. 2006). Dysregulated cortisol levels and altered stress responsiveness contribute to symptomatology in these disorders (Dziurkowska and Wesolowski 2021; Maletic and Raison 2014).

In summary, a comparative analysis of neuroanatomical features across psychiatric disorders reveals both shared commonalities and distinct neural patterns specific to each condition. Understanding these similarities and differences provides valuable insights into the heterogeneity and complexity of psychiatric illnesses, paving the way for more targeted diagnostic and therapeutic approaches tailored to individual neural profiles.

1.6 Neuroimaging Techniques and Findings

Neuroimaging methods serve as essential tools in investigating the neuroanatomy, neuropathology, and structural alterations associated with various psychiatric disorders. These techniques offer insights into the underlying neural correlates and provide valuable information aiding our understanding of the neurobiology of these conditions.

Structural MRI (magnetic resonance imaging): Structural MRI allows the visualization of brain structures and provides detailed anatomical information, enabling