Teaching Neurobiology in Psychiatry

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Abstract

The relationship between psychiatry and neuroscience has been constantly evolving since the conception of our field. The past two decades have witnessed a steep rise in research related to neurobiology in psychiatry. Advances in neuroscience have led psychiatry residency programs to steer towards a neuroscience-based approach instead of the traditional focus. Despite increased advances and interest in neuroscience and psychiatry, residency programs are not required to integrate neurobiology in psychiatry. There are several difficulties residency programs face when attempting to teach this subject area, including having availability of knowledgeable faculty, knowing what to teach, and how to deliver the information. Psychiatrists across all levels of training are enthusiastic about learning neuroscience. With the current advances in biological psychiatry, neurobiology needs to be integrated in the training and teaching of psychiatry residents. The approach of integration has to be transdiagnostic, clinically relevant, and applicable to both trainees and psychiatry educators.

We will discuss the importance of teaching neurobiology in psychiatry residency programs, outline specific areas we recommend teaching, and propose teaching strategies that may enhance learning by psychiatry residents. The neurobiology topics we recommend psychiatry programs to teach their residents include neuroscience literacy, neuroanatomy, neuroimaging, neuropathology, neural circuits and neurotransmitters, neuroendocrinology, psychoneuroimmunology, neurophysiology, genetics and epigenetics, and neuropsychological testing. There are different strategies to teach residents that enhance adult learning, which include formal discussions, clinical case presentations, journal clubs, specialized neuroscience rotations, neuroanatomy modules, grand rounds, and classes discussing topics at the interface of neuroscience and psychiatry in the media.

Keywords

Neurobiology · Teaching · Neuropsychiatry · Residency program · Adult learning · Neuroscience

Introduction

Psychiatry is the medical specialty involved in diagnosing, treating, and caring for those affected by disorders that have their pathologies directly linked to the brain and lead to emotional or behavioral conditions that affect the individual's functioning.

Neuropsychiatry is described as the clinical study of brain-behavior relationships as manifested by the psychiatric symptoms of neurological conditions and the neurobiology of psychiatric disorders (Benjamin 2013).

The relationship between psychiatry and neuroscience has been constantly evolving since the conception of our field, leading researchers to delve into the need of teaching neurobiology in residency training programs for more than half a century (Roffman et al. 2006; Rose 1966). Interestingly, during the past few decades, this bond has become much more complex and entwined. From the relationship between neurotransmitters and mental illness, to the most recent genomic and epigenetic developments, scientific advances have filled gaps in knowledge about the pathophysiology of psychiatric illnesses at such a pace, it is at times hard to follow.

The past two decades have witnessed a steep rise in research related to neurobiology in psychiatry, expanding our profession in a way we had never seen before. Advances in deep brain stimulation have allowed us to treat obsessive-compulsive disorder and neuroimaging has allowed us to visualize the neural connections and activity of healthy and ill brains, as well as help us make better clinical decisions.

Moreover, advances in neuroscience have made psychiatry residency programs steer away from the traditional focus given to residency training education with its emphasis on a more clinical framework, to a much needed neuroscience-based approach. Despite this, there are several difficulties that residency programs face when attempting to teach neuroscience. What should be taught is not clearly regulated by governing institutions and, just to add an extra layer of complexity, the material that should be taught is constantly evolving. Knowing which of the new findings will be relevant and useful in the next few decades proves to be challenging.

Another obstacle in teaching neuroscience relates to the worldwide diversity of the programs, with faculty in each institution having individual strengths, and not all programs possessing resources that include neuroscience competency. This could be addressed by recruiting faculty in departments of neuroscience, neurology, pharmacology, and other basic sciences to contribute to neuroscience teaching to psychiatry residents and fellows. Additionally, residents vary in their interest in this topic. Some of them find it complex and hard to digest, many times giving priority to other areas they believe are more clinically relevant. In a national survey by Fung et al. (2014), the group found that only a small proportion of psychiatrists across all training levels (residents, practitioners, and psychiatry department chairs) admitted to a strong knowledge base in neuroscience. This same study concluded that there is a need to bring education on this topic to psychiatry trainees and practitioners, and that this knowledge will help them provide better treatment and psychoeducation to their patients, in addition to reducing mental illness stigma.

In this chapter, we will discuss the importance of teaching neurobiology in psychiatry residency programs, outline which specific areas we recommend be taught, and propose teaching strategies that may enhance learning of this subject by psychiatry residents.

Residency Program Requirements

Despite increased global interest, exponential advances in psychiatric research, and our increasingly better understanding of the neurobiology of mental illness, the Accreditation Council for Graduate Medical Education (ACGME), which is the entity that guides the content of residency programs across the United States, does not require that neurobiology be taught and integrated in psychiatry residency training programs (ACGME 2015a). Moreover, there are multiple other requirements that residency programs may deem more clinically relevant, such as psychopharmacology or psychotherapy, which compete directly with neuroscience education.

ACGME requires that residency programs include in their curriculum a specific set of skills and knowledge, such as acquiring competency in neurological examination and knowledge of the diagnosis and treatment of neurologic disorders commonly encountered in psychiatric practice (ACGME 2015a), which are the requirements most closely related to neuropsychiatry. Table 1 presents a complete list of the mandatory requirements pertinent to neuroscience.

Table 1 Summary of ACGME-required competencies related to neuroscience

1. Medical knowledge: Residents must demonstrate knowledge of established and evolving biomedical, clinical, epidemiological, and social behavioral sciences, as well as the application of this knowledge to patient care Residents must demonstrate competence in their knowledge of:
biological, genetic, psychological, sociocultural, economic, ethnic, gender, religious/spiritual, sexual orientation, and family factors that significantly influence physical and psychological development throughout the life cycle
diagnosis and treatment of neurologic disorders commonly encountered in psychiatric practice, including neoplasm, dementia, headaches, traumatic brain injury, infectious diseases, movement disorders, neurocognitive disorders, seizure disorders, stroke, intractable pain, and other related disorders
reliability and validity of the generally accepted diagnostic techniques, including physical examination of the patient, laboratory testing, imaging, neurophysiologic and neuropsychological testing, and psychological testing
indications for and uses of electroconvulsive and neuromodulation therapies
2. Patient care and procedural skills: Residents must demonstrate competence in:
performing a physical, neurological, and mental status examination, including use of appropriate diagnostic studies
formulating an understanding of a patient's biological, psychological, behavioral, and sociocultural issues associated with etiology and treatment
3. Curriculum organization and resident experiences: Required clinical experiences:
Resident experience in neurology must include 2 months FTE of supervised clinical experience in the diagnosis and treatment of patients with neurological disorders/conditions At least 1 month of this experience should occur in the first or second year of the program

Adapted from ACGME program requirements for graduate medical education in psychiatry (2015a)

The ACGME has also implemented milestones that are designed for Psychiatry training programs to track residents' performance and progress in a semiannual review (ACGME 2015b). Table 2 sums the elements of the clinical neuroscience milestones, which include neurology, neuropsychiatry, neurodiagnostic testing, and clinical neuroscience.

In order to help residencies meet these requirements, it is mandatory for residency programs in the United States to have their residents complete a 2-month rotation on a neurology service, where they are taught these concepts. Generally, these rotations are delegated to, and managed by, the neurology department. Psychiatry residents spend 2 months working as neurology residents, commonly during their first year of training. These rotations cover basic aspects of the neurological evaluation and illnesses they see during these 2 months from a neurologic perspective. Many times

Table 2 ACGME milestones for psychiatry residency programs relevant to neuroscience

PC5. Somatic Therapies. Somatic therapies including psychopharmacology, electroconvulsive therapy (ECT), and emerging neuromodulation therapies
A: Using psychopharmacologic agents in treatment
B: Education of patient about medications
C: Monitoring of patient response to treatment and adjusting accordingly
D: Other somatic treatments
MK1. Development through the life cycle (including the impact of psychopathology on the trajectory of development and development on the expression of psychopathology)
A: Knowledge of human development
B: Knowledge of pathological and environmental influences on development
C: Incorporation of developmental concepts in understanding
MK2. Psychopathology. Includes knowledge of diagnostic criteria, epidemiology, pathophysiology, course of illness, co-morbidities, and differential diagnosis of psychiatric disorders, including substance use disorders and presentation of psychiatric disorders across the life cycle and in diverse patient populations (e.g., different cultures, families, genders, sexual orientation, ethnicity, etc.)
A: Knowledge to identify and treat psychiatric conditions
B: Knowledge to assess risk and determine level of care
C: Knowledge at the interface of psychiatry and the rest of medicine
MK3. Clinical Neuroscience. Includes knowledge of neurology, neuropsychiatry, neurodiagnostic testing, and relevant neuroscience and their application in clinical settings
A: Neurodiagnostic testing
B: Neuropsychological testing
C: Neuropsychiatric co-morbidity
D: Neurobiology
E: Applied neuroscience
MK5. Somatic Therapies. Medical Knowledge of somatic therapies, including psychopharmacology, ECT, and emerging somatic therapies, such as transcranial magnetic stimulation (TMS) and vagus nerve stimulation (VNS)
A: Knowledge of indications, metabolism and mechanism of action for medications
B: Knowledge of ECT and other emerging somatic treatments
C: Knowledge of lab studies and measures in monitoring treatment

Adapted from ACGME The Psychiatry Milestone Project (2015b)
PC Patient Care, *MK* Medical Knowledge

their instruction does not tap deeply into the overlap between both specialties but focuses only on neurological aspects of the illnesses.

In a traditional residency program, residents are taught neurobiology in an illness specific fashion during their psychiatry rotations. For example, they learn about "neurobiology of bipolar disorder" or "neurobiology of schizophrenia," and these topics would be embedded in their lectures on specific illnesses. With the current model, residents learn about neurobiology only superficially, as an add-on. In fact, a survey found that 78% of psychiatry chief residents felt unprepared to translate neuroscience research findings into clinical practice and 80% of them felt that neuroscience should be incorporated in their residency curriculum (Benett et al. 2014). For this reason, it is important to have dedicated neuroscience teaching activities focused on the details of normal neuronal and brain function that are not linked to disease. Having this as part of the curriculum in residency training programs will help residents learn the basic knowledge important to understanding the neurobiology of psychiatric diseases, paving the way for them to the next steps in learning.

Psychiatry Residents and Neuroscience

Many psychiatrists and residents in training are not commonly motivated primarily by an interest in neurobiology when choosing their careers. They normally enter this specialty attracted by the intricacies of the mind and its workings, lured by its practical clinical implications. What usually sparks their interest in neuroscience is when a clinical question leads to an explanation provided by neurobiology, thus instilling curiosity about the subject.

Psychiatry has been increasingly more popular as a choice for residency specialization in the United States, with the number of positions available increasing from 1117 in 2012 to 1384 in 2016 (National Resident Matching Program (NRMP) 2016). Furthermore, increasingly higher numbers of competitive MD-PhD students are interested in psychiatry. In Latin American countries, such as Colombia and Argentina, some universities offer psychiatric neurobiological training as part of a postgraduate program, intended to immerge biologically inclined psychiatrists into this topic. The Argentinean Association of Psychopharmacology and Neurosciences, imparts psychoneuropharmacology knowledge through a postgraduate course for interested mental health graduates with an emphasis in neurobiology. In Colombia, several residency training programs discuss this content in their curriculum and are working on having neuropsychiatry included as a postgraduate program (Holguin and Cardeno 2007).

As noted above, in the large multinational study conducted by Fung et al. (2014), only a small portion of US psychiatry department chairs, psychiatrists and trainees reported a strong knowledge base in neuroscience. However, a large portion of them were enthusiastically interested in learning neuroscience from a transdiagnostic approach, for example, emotion regulation, attention/cognition, and neural circuits. This study also found that a large portion of respondents believed that neuroscience

would help supplement new future treatments and evolve the area of personalized medicine in the next 5–10 years, as well as aid in reducing the stigma against mental illness.

Relevance of Neuroscience in Clinical Practice

The prevalence of mental illness and the morbidity and mortality associated with these disorders has been steadily increasing over the years, yet our practices and interventions have not changed all that much. It is vital that our practice in psychiatry evolves such that our treatment approaches change based on pathophysiology, in order to achieve our goal of reducing the toll of mental illness.

Neuroscience Curriculum

Currently there is no formal outline instructing which subjects should be included in a neuroscience curriculum for psychiatry training programs. The following are suggested topics that we feel should be integrated into all psychiatry residency programs, both didactics and teaching curricula, based on the most updated review of the literature.

Neuroscience Literacy

Neuroscience literacy is what the public learns and understands about neuroscience research developments usually through schooling, the media, news sources, and web-based online searches (Herculano-Houzel 2002). Neurology and psychiatry share the brain as the major mutual organ of interest. However, training and educating future psychiatrists in neuroscience continues to lag behind despite revolutionary advances in neuroscience in the past 20 years. This creates a discrepancy with patient expectations because patients now have easy access to the most recent neuroscientific advances through the media and the internet, and expect their doctors to be able to educate them about their illness from a neuroscientific perspective.

It is important for psychiatry residents to know how neuroscience's new advances are being perceived by, and communicated to, lay audiences. Psychiatrists need to act as liaisons between the information described in the media and the actual scientific information. Moreover, as academic institutions, psychiatrists are constantly requested by TV, radio, and printed news outlets to provide expert opinions on new advances in our field. Residents should be prepared to interpret this new information, be familiar with the original source, and be able to provide a clear conception of the findings to patients and other interested audiences. Understanding latest developments in neuroscience research through reading journals and being up to date with neuroscientific media coverage can aid clinicians'

understanding of their patients' cognition, emotional regulation, behavioral changes, and social encounters. Some examples of recent patient-directed questions include the indication, risks, and benefits of using cannabis, especially in the light of legalizing medical and recreational use of cannabis in some states, and also the use of ketamine in the treatment of depression. With the large number of articles written by the media and news coverage, being informed about these topics from clinical research and the media helps bridge patient education with patient perceptions from the media.

Neuroanatomy

The human brain contains 100 billion neurons that make 800 trillion connections. This organ allows the person to experience emotions, behaviors, sensations, and mediates interactions and learning from the surrounding environment. Through neuroanatomical brain imaging and postmortem studies, changes in the frontal-temporal lobes in certain dementias and changes in the limbic system in mood disorders were elucidated. Learning what is considered "normal" versus "abnormal" in brain anatomy has stemmed from mapping the brain architecture and understanding the location and functionality of the different brain structures. The long-standing classification of cerebrocortical regions by Brodmann based on cytoarchitecture has recently been supplanted by a new multimodel parcellation based on magnetic resonance imaging. This map, based on 210 healthy young adults, revealed 180 distinct cortical areas (Glasser et al. 2016). Especially important are areas suspected to be involved in major psychiatric disorder, for example, the dorsolateral prefrontal cortex (DLPFC) for executive functions and problem solving, and the orbitofrontal cortex (OFC) for regulating impulses and compulsions. It is important to understand the frontal lobe's role in executive functioning, such as motivation, attention, impulsivity, and curiosity because this helps understand the symptoms in cases of frontal lobe trauma and tumors, as well as schizophrenia, such as poor judgment, irritability, social withdrawal, and inattention. Furthermore, functional neurosurgery, i.e., psychosurgery, has been steadily growing, with deep brain stimulation being used for highly resistant obsessive compulsive disorder and more recently depression (Mayberg et al. 2016), though the latter clinical trial results have been disappointing.

Noninvasive neuromodulation procedures such as repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT) (Nuttin et al. 2014) are both US Food and Drug Administration approved treatments for major depression, especially treatment-resistant depression (Fitzgerald et al. 2012) that has not responded to antidepressants or psychotherapy. rTMS targets the right and/or left dorsolateral prefrontal cortex, whereas ECT uses a small electrical current that passes through electrodes placed on the unilateral temporal, bilateral temporal, or bilateral frontal areas to produce a short generalized seizure. This procedure is often used in both inpatient and outpatient settings to treat a variety of conditions including psychotic depression and catatonia.

Neuroimaging

In the past, psychiatric conditions were regarded as brain-related disorders in the absence of an "organic lesion" (White et al. 2012). Multiple imaging resources are currently available for psychiatrists to aid in diagnosing and differentiating among different pathologies. Studying glucose metabolism and cerebral blood flow with positron emission tomography (PET) have helped identify areas of hypo- and hypermetabolism for illnesses such as Alzheimer's disease (AD), schizophrenia, bipolar disorder, and epilepsy. PET scans utilizing specific radioactive ligands for transporters and receptors have helped elucidate the role of specific neurotransmitter systems in the pathophysiology of depression, schizophrenia, and substance abuse to name a few. In addition, specific amyloid imaging techniques are now routinely applied as adjuncts in the diagnosis of AD.

Neuroimaging techniques, especially functional neuroimaging, have reliably and repeatedly demonstrated abnormalities in the brain in psychiatric disorders. These methods such as functional magnetic resonance imaging (fMRI) may serve as trait or state biomarkers for disease. fMRI has been helpful in measuring neural activity in the presence of auditory hallucinations in patients with schizophrenia. For example, a study by Shergill et al. (2000) revealed activation in the inferior frontal insula and bilateral temporal cortex, particularly in the right hemisphere (Fig. 1). This study demonstrated activation was also present in the anterior cingulate, right thalamus and inferior colliculus, and left hippocampus and parahippocampal cortex.

Schizophrenia has been the focus of multiple imaging studies, revealing several consistent findings related to this disorder. For example, structural imaging studies using computed tomography (CT) and MRI of patients with schizophrenia, revealed enlarged lateral and third ventricles when compared to healthy matched normal comparison subjects as well as nonaffected monozygotic twins of those patients. MRI also revealed decreased cortical volume and disproportionate volume loss from temporal lobes, notably in the hippocampus. Hippocampal volume reduction has been observed and is also the focus of considerable research in patients with major depressive disorder, posttraumatic stress disorder (PTSD), Alzheimer disease (AD), and other psychiatric conditions.

Brain PET scans in patients with schizophrenia show regions of abnormal metabolic activity, with some of the most consistent findings revealing a difference in the dopaminergic neurotransmission in the anterior cingulate gyrus, the prefrontal cortex, and the hippocampus between controls and those with schizophrenia.

Structural brain imaging including CT and MRI have been an important aid in the diagnosis and progression of AD, because changes in the rate of atrophy observed in these studies strengthen the likelihood of the diagnosis, as does the finding of widened sulci and dilatation of the third and lateral ventricles in the brain. Progressive changes in brain size have been associated with longitudinal progression of cognitive loss. Moreover, disproportionate atrophy of the medial temporal lobe, particularly in the volume of the hippocampus by more than 50%, is also associated with AD. In fact, dilatation of the perihippocampal fissure is a useful imaging marker for the diagnosis of AD.

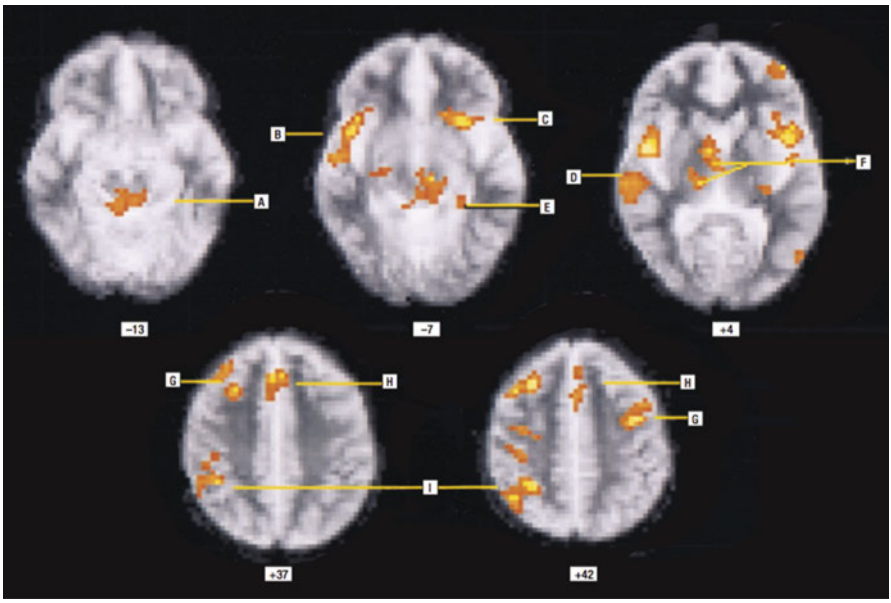

Fig. 1 Measuring neural activity in the presence of auditory hallucinations in patients with schizophrenia using fMRI. Group brain activation during random sampling of hallucinations. Five transverse sections through the brain, at different levels relative to the intercommissural plane (in millimeters). The right side of the brain is shown on the left side of each section. The colored areas are regions that were activated during auditory hallucinations, with the foci of maximal significance shown in yellow. The main activations ($P < 0.001$) were in the right inferior colliculus (*A*), the right and left insula (*B* and *C*), the left parahippocampal gyrus (*E*), the right superior temporal gyrus (*D*), and the right thalamus (*F*). Activation was also evident in the middle frontal (*G*) and the anterior cingulate gyri (*H*), and in the right inferior and superior parietal lobule (*I*). (From Shergill et al. (2000). Reprinted by permission from The JAMA Network)

In yet another striking example of the pertinence of advances of neuroscience to psychiatry are the structural and functional brain imaging applied alterations reported as a consequence of childhood maltreatment, with different subtypes of abuse and neglect producing distinct effects on particular brain regions and circuits (Nemeroff 2016). Hanson et al. (2012) studied 61 children with structural MRI and reported that increased early life trauma (ELS), as measured by the Youth Life Stress Interview, was associated with reduced prefrontal cortex volumes in both gray and white matter, specifically between the anterior cingulate and the frontal lobes, and poor executive functioning.

In a small study of young adults, Sinha et al. (2016) used fMRI to detect the central nervous system (CNS) response to stress-inducing images in order to assess coping. During active coping, the ventromedial prefrontal cortical region exhibited initial reductions in brain activation, followed by increased activation. Their study suggested that individuals who had a high risk of maladaptive coping, such as binge-drinking, emotional-eating, and being involved in more frequent fights, maintained low activity in the ventromedial prefrontal region.

A systematic review by Dichter et al. (2014) concluded that there was an association between antidepressant treatment response and neural circuit connectivity in the frontal lobe and limbic system. More recently, our group demonstrated that the interaction between early life stress and amygdala activation assessed by fMRI, in response to socially rewarding and threatening stimuli, predicted remission to escitalopram, sertraline, and venlafaxine in depressed patients (Goldstein-Piekarski et al. 2016).

Resting-state fMRI measures spontaneous brain function at rest by using blood oxygen level-dependent (BOLD) contrast in the absence of a task. This technique of neuroimaging has helped elucidate many Resting State Networks (RSN) including the somatosensory and visual networks (Lee et al. 2013). The pattern and level of connectivity in these RSNs have been studied in many psychiatric disorders including AD (Chen et al. 2011), schizophrenia (Bassett et al. 2012), and autistic spectrum disorder (Anderson et al. 2011).

Neuropathology

Postmortem brain studies have clearly shown differences between healthy brain tissue and tissue derived from patients with well-documented psychiatric disorders. It has also helped identify differences between disorders that present similarly in clinical symptoms, as for example neuropathologic differences between neurocognitive disorders. The essential neuropathologic changes in AD, including neuritic plaques, deposition of beta amyloid plaques, and neurofibrillary tangles, are quite distinct from Lewy body dementia, characterized by round, eosinophilic, intracytoplasmic neuronal inclusions (Lewy bodies), mostly clustered in the substantia nigra. Recently, postmortem studies have now confirmed the presence and rate of neurogenesis in the adult human hippocampus (Spalding et al. 2013).

Neural Circuits and Neurotransmitters

Alterations in neurotransmitter systems have been demonstrated in several psychiatric disorders. Most of the treatments available in psychiatry are believed to exert specific effects on these systems. For example, in unipolar depression, alterations in serotonin, norepinephrine, dopamine, corticotropin-releasing hormone (CRH), and to a lesser extent gamma-aminobutyric acid (GABA) and glutamate circuits have been reported.

Numerous studies have implicated multiple alterations in various components of the serotonergic system in mood disorders, including genetic polymorphisms in the promotor region of the serotonin transporter gene that interact with early life trauma (Caspi et al. 2003; Hoefgen et al. 2005) to increase depression risk, reduced plasma tryptophan concentrations (Caspi et al. 2003), the rate-limiting step in the serotonin biosynthesis pathway, and increased activity of monoamine oxidase. In clinical settings, the understanding of neural circuits and neurotransmitter changes in mood and anxiety disorders is helpful in explaining how antidepressant medications exert their desired effects as well as their unwanted side effects.

Traditionally, for example, it is taught in residency programs that dopamine acts at D2 dopamine receptors in the anterior pituitary gland to suppress prolactin secretion, and therefore typical antipsychotic drugs, as well as high doses of atypical antipsychotic risperidone, which act as antagonists at these D2 receptors, reduce psychotic symptoms but may also lead to elevated prolactin levels, which can result in amenorrhea and gynecomastia. For example, as illustrated below (Fig. 2), antipsychotics have a high affinity to a number of serotonin, muscarinic, cholinergic, histaminergic, adrenergic, and dopaminergic receptors, which are believed to mediate both their therapeutic and unwanted effects.

Understanding neurotransmitter receptor subtypes is also vital, because most psychotropic medications are selective in their effects on certain receptor subtypes. Atypical antipsychotics not only exert their main effects on dopamine D2 receptors but also on serotonin 5HT2A receptors, which are thought to possibly mediate mood stabilization and reduce extrapyramidal symptoms. However, certain atypical antipsychotics also act by antagonism or partial agonism at serotonin 5HT1A, 5HT2C, and 5HT7 receptors, which have unknown secondary effects but have been posited to contribute to anxiolytic properties (Stahl 2013). The D1 and D3 receptors are receiving much more attention lately due to their interest as putative targets in treatment of psychosis.

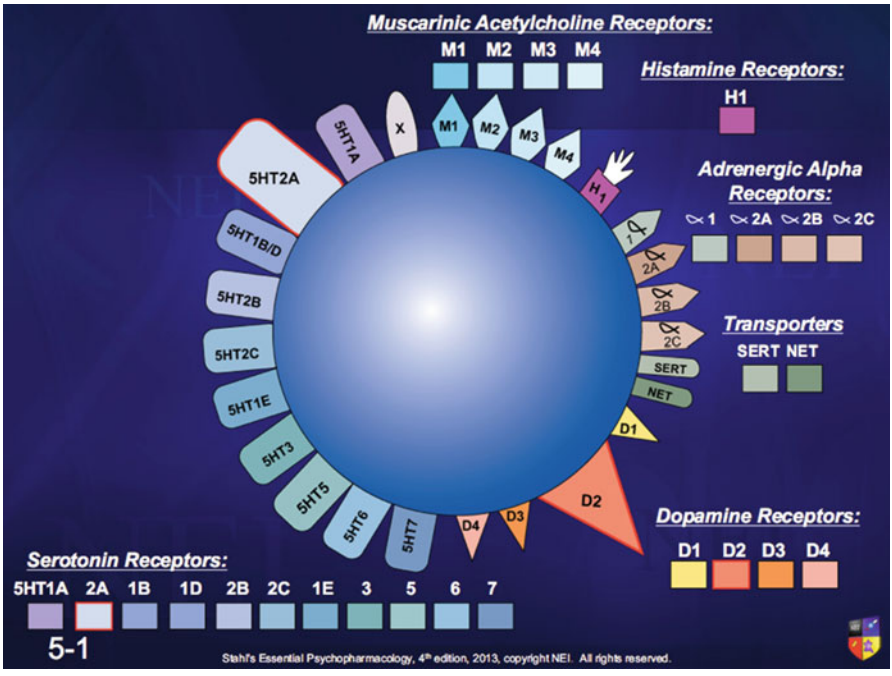

Fig. 2 Antipsychotics have high affinity to a number of serotonin, muscarinic acetylcholine, histamine, adrenergic, and dopamine receptors. (From Stephen M. Stahl (2013). Reprinted by permission from Stephen M. Stahl, copyright Neuroscience Education Institute)

Neuroendocrinology

It has long been known that the endocrine system and the CNS interact in a complex fashion which affects emotions and behavior. The thyroid axis certainly plays a critical role in the pathophysiology of mood disorders with occult primary hypothyroidism representing the number one medical cause of depression. Another cause of depression in men is testosterone deficiency. A significant minority of depressed men who are hypogonadal are returned to euthymia by testosterone replacement alone. Oxytocinergic systems, which play a major role in social bonding, attachment, sexual pleasure, and lactation, have been reported to be altered in mood and anxiety disorders, especially in victims of child abuse and neglect.

The most widely studied endocrine system relating to stress and stress-related psychiatric disorders is the hypothalamic-pituitary-adrenal (HPA) axis, and numerous studies have implicated a seminal role for this system in depression (Gillespie and Nemeroff 2005), anxiety disorders and PTSD.

Assessing HPA axis function includes measuring basal hormone levels or by provocative challenges, such as the dexamethasone suppression test or the CRH stimulation test. A substantial number of depressed patients fail to suppress cortisol secretion when challenged with the synthetic glucocorticoid dexamethasone, which reflects feedback regulation impairment and hyperactivity of the HPA axis (Nemeroff 2016). The degree of change in the HPA system in relation to early life trauma is influenced by a number of factors, which include: the nature, frequency, age of onset of the trauma, availability and access to psychosocial support, later life trauma, family history of mental illness, and genetic and epigenetic contributions. This hyperactivity of the HPA axis is in part due to hypersecretion of CRH, which has now been unequivocally shown to occur after exposure to child abuse and neglect. It is also well known that the iatrogenic use of hormones, or hormone derivatives such as cortisone, may lead to side effects that manifest as depression, mania, or psychosis (Brown and Chandler 2009; Dubovsky et al. 2012).

Psychoneuroimmunology

Since the 1980s, research has burgeoned in the area of psychoneuroimmunology, which revealed complex interactions between the brain and the immune system. Several studies have demonstrated an increased rate of depression in disorders characterized by increased inflammation such as cancer, diabetes, and ischemic heart disease. Moreover, multiple studies have shown higher concentrations of inflammatory markers in patients with depression, including cytokines IL-1, IL-6, tumor necrosis factor α (TNF α), and C-reactive protein (CRP) (Howren et al. 2009). A meta-analysis revealed significantly higher concentrations of the proinflammatory cytokines TNF and IL-6 in depressed patients compared to controls (Dowlati et al. 2010). This effect is particularly prominent in suicidal patients. There is increasing evidence that certain anti-inflammatory agents may possess antidepressant properties (Raison et al. 2013).

The Adverse Childhood Experience (ACE) study was one of the first and largest studies that illustrated the association between childhood trauma and an increased risk for a variety of inflammatory medical conditions including ischemic heart disease, cancer, chronic obstructive pulmonary disease, asthma, obesity, autoimmune disease, and liver disease. Danese et al. (2008) completed a large prospective longitudinal cohort study to determine whether a history of childhood abuse in depressed patients resulted in elevated levels of CRP and other markers of inflammation. Their group assessed approximately 1000 subjects that were followed to age 32 in the Dunedin Multidisciplinary Health and Development Study for a history of childhood maltreatment and subsequent medical and psychiatric disorders. Children with a history of childhood maltreatment exhibited a significant increase in CRP concentrations that continued throughout adulthood; this was independent of other risk factors including depression, low socioeconomic status, poor health, or smoking. This study has subsequently been confirmed in a large meta-analysis (Baumeister et al. 2016).

Neurophysiology

Understanding neurophysiology and electrophysiology aids in the use, understanding, and interpretation of results of electroencephalograms (EEGs), which are used to rule out epilepsy as a cause of psychiatric symptoms, as well as during ECT and in the diagnosis of sleep disorders. Deep brain stimulation, which is FDA-approved for treating resistant obsessive-compulsive disorder (Kisely et al. 2014), uses an electrophysiological technique known as microelectrode recording (MER) to micro-tune the specific target site locations. During this procedure, electrodes are slowly advanced to targeted brain structures, which are identified based on the patterns of electrode firing. This involves not only knowledge of neurophysiology but in neuroanatomy as well. EEG also holds the promise for identifying subtypes of patients with schizophrenia and mood disorders, as well as predicting optimal treatment response.

Genetics and Epigenetics

Genetics has played a seminal role in the development of personalized or precision medicine, especially in oncology, where detecting gene mutations has predicted both disease risk and treatment response. Genome-wide association studies (GWAS) in psychiatry (Kim et al. 2017) have detected genetic variants of disease, e.g., single nucleotide polymorphisms (SNPs) or copy number variations (CNVs), that contribute to disease vulnerability. Genetic linkage studies preceded GWAS and identified certain genetic markers in specific chromosomal regions associated with disease vulnerability. It was used to obtain information from large families with heritable illnesses, and samples are obtained from family members with and without the specified disease. These advances preceded GWAS and were somewhat informative in bipolar disorder,

major depression, and schizophrenia. GWAS, however, identified several gene variants, each of which exerts a small but significant effect on disease vulnerability but are far less clinically impactful as single-gene mutations in Mendelian inherited illnesses such as Huntington's disease and cystic fibrosis.

In a review of personalized medicine and mood disorders (Alhajji and Nemeroff 2015), we noted that the approximate lifetime prevalence of Major Depressive Disorder (MDD) in women is more than tripled in those who have a significant family history. Bipolar disorder is one of the most heritable psychiatric illnesses with a strong familial component that increases the risk up to 10 times. Indeed, two thirds of the risk of development of bipolar disorder is hereditary. Genetic polymorphisms in the serotonergic system, including serotonin transporter (5-HTT) gene and components of the HPA axis system such as the corticotropin-releasing hormone-binding protein (CRHBP) and FK506-binding protein (FKBP5) genes have been repeatedly implicated in the susceptibility to developing major depressive disorder. Although several commercial laboratories offer genetic testing to predict antidepressant response, our view is that these tests are not yet sufficiently validated for widespread use.

Epigenetics is likely the fastest growing field in all of biology, including neurobiology. It encompasses heritable genetic changes that are due to factors other than changes in the DNA sequence. This includes processes that regulate gene transcription, such as DNA methylation and histone modification. FKBP5 is a co-chaperone of the heat shock protein-90 (HSP90) in the mature glucocorticoid receptor complex. It codes for a protein that causes glucocorticoid receptor subsensitivity (Binder et al. 2004). Depressed patients who are homozygous carriers for the rs1360780 SNP of FKBP5 respond more rapidly to SSRIs, TCAs, and mirtazapine, compared to non-carriers (Binder et al. 2004). Our group illustrated that the risk allele of the FKBP5 gene, which is regulated by epigenetic processes, determined the likelihood of developing PTSD in adults with a history of child abuse (Klengel et al. 2013), and this effect is mediated by epigenetic changes in the risk allele. Epigenetic alterations as a consequence of child abuse and neglect and their role in mood disorder vulnerability and in particular the risk for suicide is an active avenue of investigation.

Neuropsychological Testing

Neuropsychology is a subdiscipline of psychology that specializes in identifying brain-behavior relationships by assessing cognitive and emotional brain functions and their role in a person's behavioral manifestations and daily functioning. Neuropsychological assessment involves administering a battery of tests that serve to identify areas that may be dysfunctional and may be associated with a particular neurological or psychiatric disorder. The results of most of these assessments use normative data to determine a person's strengths and weaknesses. In order for a provider to administer and interpret neuropsychological testing, and be able to provide a therapeutic discussion with a patient, one must be knowledgeable of the underlying neurobiology.

Indeed, neuropsychological testing is particularly useful in identifying patients with cognitive impairments, where specific tests can be used to assess attention, orientation, executive function, verbal memory, spatial memory, language, and motor/sensory functions. The Trail Making Test (TMT) is valuable in providing information regarding visual scanning, simple visual span of attention, speed of processing, mental flexibility, and executive functioning. It consists of two parts, TMT-A which involves having the subject connect lines in a sequential matter between 25 encircled number, whereas in TMT-B the subject must alternate connecting lines between numbers and letters. As with any neuropsychological test, TMT results may be affected by age, education level, and intelligence. The Wisconsin Card Sorting Test is a commonly used instrument to detect executive dysfunction such as the difficulty with problem solving and mental flexibility that occur in schizophrenia. Tests such as Block Design Test and Clock Drawing Test may detect visuoconstructional abilities and apraxia in patients with Alzheimer's Dementia and Frontotemporal Dementia.

Children and adults with Attention Deficit Hyperactivity Disorder (ADHD) not only present with problems with attention, hyperactivity, and impulsivity but also may display a combination of developmental deficits in learning, language, visuomotor processing, or auditory processing domains. With ADHD implicating different domains, there are many objective tests that can be used with varying degrees of sensitivity and specificity. Behavioral symptoms can be assessed by using the Behavior Rating Inventory of Executive Function (BRIEF), attention can be tested by using the Continuous Performance Test or Go/No Go Test, planning and organizational thinking using the Tower of London Test, while intelligence and abstract reasoning can be evaluated using the Wechsler Adult Intelligence Scales. Used in combination with parent and teacher as well as self-rating scales, ADHD can be reliably diagnosed with sensitivity and specificity far better than unstructured clinical evaluations.

Teaching Strategies

Due to the wide range of mandatory topics lined out by the ACGME, it may be relatively difficult to fit neuroscience topics into the didactics curriculum. It is vital that the neuroscientific material that is taught to residents in class is applied to clinical settings, because not doing so would enforce the message that neuroscience is not important in patient care (Hafler et al. 2011). Our aim is to integrate neuroscience into engaging and clinically relevant teaching strategies and educational modalities, as it has been shown that traditional lectures are only 5% effective in conveying information to adult learners (Stahl and Davis 2009).

Neuroscience Rotation

As mentioned earlier in this chapter, during the neurology rotation of psychiatry residency training, psychiatry residents work as neurology residents for

a period of 2 months and take part in the other department's clinical and academic activities. Often a link between both specialties is not stressed during the rotation, and the goal of integrating neuroscience into psychiatry is not entirely met.

For this reason, some programs have proposed creating a specific neurobiology rotation that integrates neurobiological aspects of psychiatry into a neurology experience. This proposal would include a specific academic curriculum in which topics related to the interface of psychiatry and neurology would be incorporated. We are enthusiastic about this approach, but it might be difficult to accomplish at some sites. The programs that do this successfully will have a cohort of neurobiologically well-educated psychiatrists compared to other programs.

A tailored clinical experience, either on an inpatient unit or in the outpatient setting, where the patient population is comprised of those with neurological illnesses that may manifest with psychiatric symptoms, is another possible approach of integrating both specialties in a worthwhile experience. This would require joint efforts from both departments and would positively enhance opportunities of learning among residents in both specialties. A multidisciplinary team with the participation of an attending faculty neurologist and psychiatrist familiar with the neurobiological aspects of psychiatric illnesses would be ideal.

Among the benefits of this type of rotation, residents would be able to learn how to explain to patients the underlying neuropathogenesis of their diseases. Neurology, neuroimaging, neuropathology, and new research findings would be included in their day to day practice, providing an opportunity to integrate neurobiological theories into clinical activities. It is not surprising that many of our most successful psychiatric investigators are dual boarded in psychiatry and neurology.

Classes

For many decades, education has been delivered through lectures, which until recent times have been considered the standard form of teaching. In this modality of information delivery, speakers normally tend to provide as much information as they can in a limited time, making sure everything that the student needs to know is covered in their lecture. We all have taken part in these types of classes in one way or another, either by teaching them or, most probably, during our days in elementary school, high school, and college.

This type of approach to teaching might not be the optimal method for adults to learn new information, as it has been shown that adult learners may pay attention to a lecture for only 15–20 min at a time, specifically at the beginning of the presentation (Stahl and Davis 2009). After this time, attention span dwindles, making it less probable that learning will occur. Strategies aimed at constantly changing the pace of a presentation in order to keep audiences attentive have been shown to improve retention of the newly learned information. This includes, but is not limited

to, the use of clinical cases related to the topic being taught, encouraging those participating to think about different ways to use the information provided in a practical way.

The use of traditional lectures is being revisited in most academic institutions. Many medical schools have done away with those types of presentations in which the audience has little to no participation and have replaced them with more interactive ones where different mechanisms provide a means to engage the student and help enhance the learning process.

Advanced technology has enhanced the way feedback is obtained from audiences in a classroom in a dramatic way. Rather than a traditional show of hands, when asking a question that involves multiple possible answers during a lecture, it is now easy to use audience response systems on phone applications connected to a presentation to obtain a real live recount of the audience responses. After a few seconds, the answers appear on screen and may even be displayed in a graph. Nowadays, all residents own a smartphone or a tablet, making it possible for the faculty member lecturing to have the residents connect their devices to the presentation. This offers the opportunity of obtaining immediate answers to the questions being made, providing residents immediate feedback. This will help the lecturer decide if he or she needs to move on with the class if the topic is understood by the majority of the group, or if more time should be spent on the subject if the opposite is true.

When teaching medical content, especially neurobiology in psychiatry, it is important to consider several elements and ask ourselves questions such as: Which is the target audience? How much information is being provided in a single presentation? Is it too much content for one class? Are clear and relevant graphical displays being used? Is the audience being stimulated appropriately? All of the answers to these questions will provide clues as to how to deliver effectively the required information residents need to learn during their training, making it an experience worthy of their time. Effective classes will not only provide the needed information but will hopefully instill in the resident interest in knowing more about the topics being taught.

When referring to clear and relevant graphical displays while giving a lecture, Stahl and Davis (2009) recommend using enhanced contiguity and providing a stepwise appearance of labels when teaching about anatomical structures, specifically when their function is being explained. Adults learn concepts better when corresponding words and images are presented in close proximity instead of far from each other on the screen. As Figs. 3 and 4 show, when describing the function and location of the different structures of the brain, having all the information placed on a single slide will not help those attending the class learn the information. If a stepwise appearance of words describing the name of the structure and its function occurs simultaneously and these words are in close proximity to the structure being described, learning will be enhanced.

Overall, teachers need to understand that the focus of medical education is the person learning, not the teacher. Attention should be given to faculty involved in residency teaching, giving them the opportunity to develop strategies to develop presentations that include components more in line with adult learning theories.

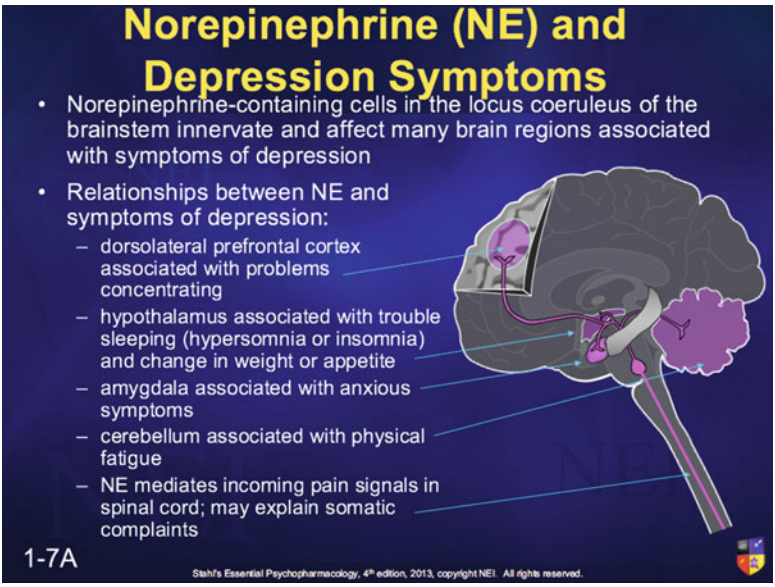

Fig. 3 Displaying abundant information on a single slide is not helpful in learning new information. (From Stephen M. Stahl (2013). Reprinted by permission from Stephen M. Stahl, copyright Neuroscience Education Institute)

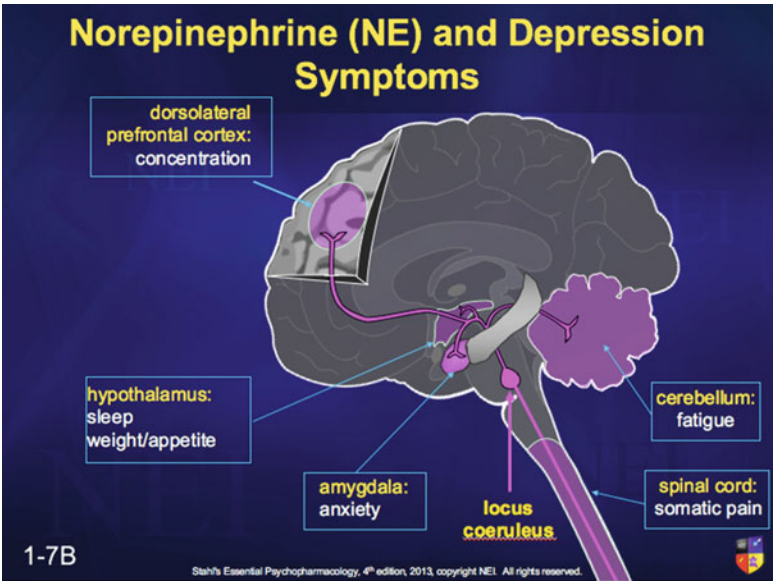

Fig. 4 A stepwise appearance of the name and function of a structure with keywords being in close proximity to each other enhances learning. (From Stephen M. Stahl (2013). Reprinted by permission from Stephen M. Stahl, copyright Neuroscience Education Institute)

This will help teachers offer an adequate experience to residents, making it valuable for them, and providing them with information that is relevant, useful, and applicable to their practices.

Journal Clubs

Training programs across all medical specialties include in their curriculum weekly or monthly journal clubs, where an article of relevance is discussed among faculty and residents. This academic activity meets several goals important for the trainees' learning. Among these goals, teaching residents appraisal skills aimed at analyzing a scientific paper is a very important one. As mentioned earlier, residents are constantly bombarded with the influx of new information on a multitude of topics currently being studied, and it is not an easy task to decide which will be relevant. It is key for them to critically read these papers and discern between studies performed in an appropriate manner and those that are not. Residents are guided on how to develop their own critical thinking of the literature.

Another goal in discussing and analyzing scientific papers is for this exercise to impact on their clinical practice. Indeed, this must entail the use of evidence-based medicine derived from controlled studies. Discussing landmark papers that have transformed psychiatric practice in journal club highlights the optimal treatments for their patients. It will also further help them understand from a neurobiological perspective the nature of their patients' illnesses, and translate this knowledge into terms patients will be able to understand.

Having a dedicated journal club activity also aids in keeping residents and faculty up to date with the current literature. Due to the plethora of new neuroscience information developing every day in our field, it is difficult for many to keep up to date on all the new advances. One might even establish a neurobiology journal club, per se.

Taking all these points into consideration, the psychiatry residency program at the University of Miami has been using a model that consists of a longitudinal journal club series where a compendium of landmark papers are prepared by two or three residents and are guided by an experienced faculty member. The selected paper is then presented to the rest of the trainees and faculty members. The specific papers to be discussed have been previously selected by a committee comprised of faculty involved in the yearlong journal club series as mentors and are chosen based on the relevance of the paper to a psychiatrist's clinical practice and the potential for neurobiological discussion. These landmark studies are presented during the first half of the series and revisited every 2 years to make sure all residents are exposed to them. Later on in the year, selected papers with identified flaws are prepared by a group of psychiatry trainees and a mentor, with the goal of learning how to identify potential issues in the development and analysis of scientific research. Residents are expected to read the articles and be able to point out the errors in the paper. Additionally, recently published papers with relevant neurobiological content are presented during this activity, giving the

residents the opportunity to learn about newer advances in the field while critically appraising a scientific publication.

Grand Rounds

Across the various residency programs in the United States, grand round activities are held in diverse fashions and different schedules. Some are more neurobiologically inclined than others, but all have the goal of bringing faculty and residents of the department together in a stimulating academic setting. At the University of Miami Miller School of Medicine, grand rounds are managed in a state-of-the-art fashion, with an ongoing series of scholarly lectures given by world-renowned experts in the field. The speakers are departmental chairpersons of prestigious universities, eminent scholars, and distinguished professors from the most renowned medical schools and research institutions in the United States. They address during their presentations issues aligned with the most recent developments in basic neuroscience and in the diagnosis and treatment of psychiatric disorders, emphasizing the neurobiological aspect of their work, presenting their latest research results and the most up-to-date advances in patient treatment modalities. This activity is extremely interactive and intellectually stimulating for our residents, as they not only get the opportunity of participating during their presentation but also have a time reserved to share lunch with the speaker in a more relaxed setting. Residents are provided with the unique opportunity of having a one to one, more informal interaction with the presenter, where possibilities for clarification of concepts, development of research questions, future collaborations, and lifelong friendships take place.

Case Formulations, Vignettes, and Discussions

Assessing patient cases from an integrative neurobiological, psychological, and social perspective increases the understanding of the patient's complex psychopathology and renders learning neuroscience clinically relevant for residents. It also allows for clinical applications in a multitude of patient settings, including inpatient, outpatient, and residential.

As noted previously, a group at Stanford University assessed the attitudes of chairs of psychiatry departments, psychiatrists, and psychiatry trainees' attitudes towards neuroscience education (Fung et al. 2014). In that study, psychiatry trainees found case conferences and clinical-based teaching significantly helpful. In a progressive 4-year long neuroscience curriculum developed for psychiatry residents at Yale University (Ross and Rohrbaugh 2014), a "multi-perspective case conference series" was developed for postgraduate year (PGY) 2 residents. In this series, a wide variety of psychopathologies written and verbal case formulations were presented from a neurobiological, psychological, and social approaches. The residents interacted with expert faculty members and received peer supervision, with the

goal of writing up at least one patient during the course, and then presenting their case to a diverse panel that includes a neuroscientist, a psychotherapist, and a social psychiatrist for comment and feedback.

The US National Institute of Mental Health (NIMH) has created free online neuroscience modules (NIMH 2012a, b) that link core educational information to a clinical case and provide clinical formulation and problem solving.

Neuroanatomy Modules

The National Neuroscience Curriculum Initiative (NNCI 2013) is an organization that was initially formed by psychiatry residency training directors from Columbia, Brown, Pittsburgh, and Yale that is funded by the US National Institute of Health (NIH) to create collaboration between educators and neuroscientists. Their aim is to supply and create clinically applicable resources that help train psychiatry residents in neuroscience. This includes a collection of interactive learning modules that trainees could use to supplement their learning in the classroom, in clinical settings, and in self-directed studying. This curriculum is updated and adapted from curricula that are already implemented in psychiatry residency training programs nationally and internationally.

Their first initiative, The Play-Doh brain (Ross et al. 2016), is a tactile-based learning exercise that introduces learners to the neuroanatomy of the brain. In this activity, learners recreate the gross anatomy of the brain using Play-Doh material and in the process learn the basic function of each structure. With the prolific and wide use of smartphones, a variety of interactive applications have also been developed to teach neuroanatomy, such as 3D Brain ©, Brain Tutor ©, and Draw:Know ©.

Cold Spring Harbor Laboratory has developed a website called Genes to Cognition (2017) which includes the 3D Brain program, along with other interactive learning and teaching modules. The 3D brain encompasses an interactive three-dimensional model of the brain, subdividing it into clickable brightly colored lobes, brainstem, and cerebellum. Within each brain structure is a further colorfully divided subsections, such as Broca's area, prefrontal cortex, premotor cortex, and primary motor cortex under the frontal lobe. When clicking at the brain as a whole, or at each section, a concise but well-rounded write-up pops up and provides information of the following: an overview, case studies, associated functions, associated cognitive disorders, associated with damage, substructures, research review, and links relevant to the particular structure.

Neuroscience in the Media

Under one of The National Neuroscience Curriculum Initiative's (NNCI) classroom, modules, titled "Fundamentals of Neuroscience", is a subsection called Neuroscience in the Media. This aims to teach residents to explore the interface between

psychiatry and the media, and to learn how to translate findings from clinical research to a lay audience. In these sessions, each begins by reviewing a media piece relating to psychiatry and neuroscience or the residents can be given the freedom to pick their own item of media coverage. The sessions are then structured to provide criticism of the piece, discussing related clinical research, and role-playing discussing this topic to a lay audience while eliminating the use of excessive medical jargon. Amongst many of their suggested topics are the following: "Are Probiotics the New Drug Choice for Mental Illness?", "Effects of Marijuana on the Developing Brain", "How Social Media Changes Your Brain," and "The Effects of Emotions on Memory Accuracy."

The Yale psychiatry residency training program (Ross and Rohrbaugh 2014) has also integrated a neuroscience literacy component to their neuroscience curriculum titled "NY Times Psychiatry." This 6-week long course for PGY-4 residents allows them to research and select relevant articles in the media for critical appraisal and for understanding how to transmit clinical findings to lay audiences. Other options would include watching movies or reading fictional books and discussing their medical accuracy and societal portrayal.

At the University of Miami Miller School of Medicine, faculty, residents, and medical students participate in movie screening nights through the psychiatry special interest group, a medical student organization aimed at sparking interest in psychiatry among the medical students. Watching and discussing movies with psychiatric content among peers at different levels of training fulfills various purposes. From the academic point of view, topics such as diagnosis, neurobiology of the illness, and possible management strategies are discussed, making this a learning and fun experience for students and residents which is distinct from their regular undertakings. This activity also contributes to helping our trainees understand the different ways psychiatry is being portrayed on screen, and how the lay audience perceives and may interpret these illnesses.

Conclusion

Because neuroscience is the basic science of psychiatry, it must be an integrated component in the training and teaching of psychiatry residents. This can be accomplished through department chairs and academic leaders who are involved in large-scale committees in charge of creating the ACGME educational requirements, milestones, the US Psychiatry Resident-In-Training Examination (PRITE) exams, psychiatry board certification, or smaller departmental committees such as journal clubs, case conferences, grand rounds, or classes. The approach of integration has to be transdiagnostic, clinically relevant, and applicable to both trainees and psychiatry educators.

As previously noted, psychiatrists across all levels of training are enthusiastic about learning more neuroscience. To further encourage and motivate residents who

are interested in neuroscience, special recognition should be provided to residents who contribute to neuroscience research or education.

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Board of Directors: AFSP, Gratitude America, ADAA
Income sources or equity of $10,000 or more: American Psychiatric Publishing, Xhale, Bracket (Clintara), CME Outfitters, Takeda
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