Exploring psychotherapeutic issues and agents in clinical practice

Genetic and Environmental Contributions to Mental Illness With Implications for Evaluation and Treatment

EDITOR'S NOTE

I am honored to take on the role of Psychopharmacology Section Editor for the Journal of Psychosocial Nursing and Mental Health Services, and very grateful to our previous Editor, Barbara Limandri, PhD, PMHNP, BC, for her mentorship. What drew me to the Journal was her in-depth coverage of neurophysiological abnormalities associated with mental disorders and how they are targeted by psychotropic medications. I hope to continue that tradition and I welcome submissions and ideas from readers.—K. Kverno



ABSTRACT

From the outside looking in, it may appear that nurse practitioner practice in mental health care is relatively easy compared to other nurse practitioner population care. The current article presents a brief overview of recent theories on the etiology of mental disorders, specifically major depressive disorder, bipolar disorder, and schizophrenia, with implications for practice. Pharmacological treatments targeting important stress response and immune and inflammatory targets lag behind the science. A practical framework for psychiatric evaluation, formulation, and treatment planning that combines four distinctive ways of viewing patients' concerns is presented as a useful method for providing person-centered mental health care. [Journal of Psychosocial Nursing and Mental Health Services, 59(1), 9-13.]

was recently struck by an off-hand comment by a colleague who made an unfavorable comparison between psychiatric-mental health nurse practitioners (PMHNPs), who just talk to people, and acute care nurse practitioners who do the more complicated work of caring for critically ill patients. It is true that in psychiatry, we can only understand a patient's thoughts and emotions through dialogue-yet psychiatric illnesses can be just as critical in terms of life or death.

Intentional suicide was the 10th leading cause of death in the United

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Psychopharmacology

States in 2017 and 2018 (Xu et al., 2020). Chronic and recurrent mental illnesses, such as major depressive disorder (MDD), bipolar disorder, and schizophrenia, generally start within the first 2 decades of life and are common causes of disability (Healthy People.gov, 2020). The pathogenesis of these disorders, and finding new, more effective treatments is, as the former director of the National Institute of Mental Health (NIMH) and Director of the Stanley Center for Psychiatry Research, Dr. Steve Hyman (2018, p. 4) stated, "fiendishly complex."

ETIOLOGICAL HYPOTHESES

Twenty years ago, I attended a symposium in Washington, D.C., of brief presentations given by brain science researchers that had been funded through the Decade of the Brain initiative of the Library of Congress and the NIMH. There was an exciting sense that understanding the underlying pathophysiology of common mental disorders was within reach. Hypotheses about abnormalities involving specific monoamine neurotransmitters (serotonin, norepinephrine, and dopamine) at specific receptors in specific structures and pathways that served specific functions included the monoamine-related hypotheses of MDD (Delgado, 2000; Maffioletti et al., 2020) and the dopamine dysregulation hypotheses of psychosis associated with bipolar disorder (Ashok et al., 2017) and schizophrenia (Howes et al., 2017; Jauhar et al., 2017).

Although today much more is known about the mechanisms of these illnesses, with the exception of lithium and the antiepileptic drugs for bipolar disorder, our first-line treatments for MDD, bipolar disorder, and schizophrenia still target one or more of the three monoamines. The medications are all effective in treating target symptoms and syndromes to some degree; however, there have been few pharmaceutical breakthroughs and the actual etiopathogenesis of mental disorders appears to be a much more complicat-

ed puzzle that involves multifactorial interactions between genetic vulnerabilities and social, psychological, and biological factors (Fang & Mao, 2019; Hyman, 2018; Liu et al., 2020).

Genetics

The heritability of MDD, bipolar disorder, and schizophrenia is high (Ozomaro et al., 2013), but not through disorder-specific genetic risks (Hyman, 2018). Instead, mental disorders are thought to result from extreme polygenicity, involving thousands of genes with overlapping genetic risk across disorders (Fang & Mao, 2019; Hyman, 2018). Schizophrenia and bipolar disorders share approximately 65% of their common risk alleles (i.e., forms of a particular gene), suggesting that it is the diverse patterns of shared and unshared genetic risks that differentiate the mental disorders, not the categorical sets of symptoms that appear in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5) (American Psychiatric Association, 2013; Hyman, 2018). Rather than a categorical method of diagnoses, some have suggested that a dimensional approach, along the axes of affect, psychosis, and cognition would be more in line with the state of science today (Liu et al., 2020; Öngür, 2017).

Socio-Environmental Context

The first two decades of life are a period of brain development and modification through the dynamic associations among cognitive, biological, and environmental factors. It is during this time that secure attachment relationships and social interactions are key factors in shaping social competence, affect management, and resilience (Centers for Disease Control and Prevention [CDC], 2020; Tuerk et al., 2020). During this period, early adverse childhood events, such as physical abuse or neglect, are known to hinder brain development and increase the risk for mental health problems or disorders in adulthood (CDC, 2020;

Schouw et al., 2020). A vulnerability-stress-inflammation more posits that chronic stress may increase hypothalamic-pituitary-adrenal axis dysregulation and activate the immune system, leading to chronic inflammation and increasing risk for cognitive, affective, and physical illness (Maydych, 2019; Müller, 2018; Sapolsky, 2018; Troubat et al., 2020).

Intersections Between Genes and Environment

Large cohort studies in the Netherlands have shown that intergenerational transmission of traits and behaviors results from interactions between genetic and non-genetic factors (Branje et al., 2020). Genes influence how people react to the sociocultural environment and how the sociocultural environment affects physical, brain, and personality development and health.

One of the most interesting areas of current research regarding the etiopathogenesis of mental disorders focuses on interactions among genes, a loss of microbial diversity in the gut (dysbiosis), and changes in central nervous system (CNS) development and function. Microbiota-gut-brain hypotheses posit that shifts in the natural microbiome, either prenatally or afterward, result in microglial (CNS immune cell) activation that triggers neuroinflammation that can interfere with normal brain functions in people who are genetically predisposed. Microbiota-related neuroinflammation is proposed as a potential pathogenic component in MDD (Carlessi et al., 2019; Evrensel et al., 2020) and schizophrenia (Severance & Yolken, 2020), and perhaps less clearly for bipolar disorder (Benedetti et al., 2020; Flowers et al., 2020).

IMPLICATIONS FOR THE PMHNP

Abnormal symptoms, behaviors, and reactions have etiologies, but unlike other areas of medical practice, we do not have laboratory studies, di-

agnostic tests, or scans to pinpoint the pathophysiology—and the etiology is most likely the result of complex geneenvironmental interactions. Talking with patients—that is, establishing a therapeutic relationship with our patients—is the first step toward gaining a thorough understanding of the history and current problems and synthesizing the information into a concise explanatory impression/formulation. The use of an overarching framework for this process of psychiatric evaluation and formulation is helpful for accuracy of diagnosis and collaborative treatment planning. One such framework is the Perspectives of Psychiatry that evolved out of 100 years of research and practice at Johns Hopkins University (Chisolm & Lyketsos, 2012; DePaulo, 2017; McHugh & Slavney, 1998). The Perspectives are four ways of viewing potential contributions to a patient's condition: (1) disease: what the patient has; (b) dimensional: who the patient is; (c) behavior: what the patient does; and (d) life story: what the patient has encountered. Using the Perspectives, we ask ourselves the following ques-

Does the patient have a psychiatric disorder? Using the Perspectives framework, history of mental illness in the patient or family and history of an early mood episode or psychotic episode with recurrent or persistent symptoms fit a disease construct. In current practice, the question is also: Does this patient fit the categorical criteria for a specific DSM-5 disorder? Best practice guidelines provide us with first-line options for treatment of specific mental disorders, and the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial results remind us that remission of symptoms may be a process that takes time and may involve a trial of more than one medication or augmentation (Rush et al., 2006; Trivedi et al., 2006).

Pharmacogenetic testing and pharmacogenomic testing have limited uses in psychiatric care. In a review and con-

sensus statement, the International Society of Psychiatric Genetics (Bousman et al., 2020) concluded that evidence supports the use of pharmacogenetic testing in relation to cytochrome P450 2D6 and 2C19 enzymes to determine metabolizer phenotypes ranging from poor to ultrarapid and to inform medication selection and dosing of some of the commonly used antidepressant and antipsychotic medications. They also support pharmacogenetic testing in genetically at-risk populations (e.g., Han Chinese, Thai, Vietnamese, Indonesian, Malay, Filipino, or Indian descent) for the immunologic human leukocyte antigen genes HLA-A and HLA-B prior to using some antiepileptic mood stabilizers. Specific variants of HLA-A and HLA-B are known to increase the risk for severe cutaneous adverse reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis). (See Amato et al. [2018] and White et al. [2019] for recent overviews.)

What are the patient's cognitive and temperamental strengths and vulnerabilities? How people interpret and react to life events is based on their intellectual capacity and personality (DePaulo, 2017; McHugh & Slavney, 1998). In contrast to the DSM-5 categorical descriptions of personality types, a dimensional approach may be more useful to understanding individual differences in reactivity, intensity, and duration of responses to emotional stressors (McCrae & Costa, 1987; Rein & Eysenck, 1953). All people fit somewhere on each trait dimension (e.g., extraversion, neuroticism, openness, conscientiousness, agreeableness). The combinations/interactions across trait dimensions describe who the person is. Personality traits should be considered in relation to the presenting problem, as potential predisposing factors and protective factors (Crescentini et al., 2018; Macneil et al., 2012). In relation to treatment, personality traits have been linked to treatment adherence (Hazrati-Meimaneh et al., 2020), medication overuse or avoidance (Mohseni et al., 2017), and trajectory of symptom change (Aluoja et al., 2018). In addition, clinician personality traits related to risk tolerance and ambiguity can impact medication decision making, risk for medication errors, and patient outcomes.

What are the patient's coping skills? Behavioral patterns are considered potential perpetuating or protective factors in relation to what the person has (presenting problems) and in response to stressful life events (DePaulo, 2017; Macneil et al., 2012; McHugh & Slavney, 1998). Behaviors are highly influenced by temperament. For example, people high in introversion may be more likely to avoid situations that cause discomfort. People high in extroversion may be more impulsive and engage in more high-risk coping behaviors. Using the behavior perspective approach, the treatment plan for maladaptive behaviors is to interrupt maladaptive behaviors and strengthen positive coping skills, stress management, and resilience (Chisolm & Lyketsos, 2012). Avoidance or withdrawal, substance misuse, and other maladaptive coping behaviors can be effectively treated with cognitive and behavioral therapies, such as dialectical behavior therapy (Fassbinder et al., 2016).

What is the patient's life story and personal narrative? The life story perspective may help us understand social and environmental predisposing and precipitating factors. Life events can be predisposing factors, such as traumatic events that put a person at risk for developing a mental disorder. Life events may also be precipitating factors, such as interpersonal or financial stressors, that are outside of a person's perceived capacity to cope or adapt. It is our job as clinicians to help our patients find meaning from their life stories, including the sequence of life events, personal responses, and outcomes. A traumainformed approach to care defined by the Substance Abuse and Mental Health Services Administration (2014) requires the clinician to realize

Psychopharmacology

the widespread impact of trauma and understand potential paths for recovery; recognize the signs and symptoms in our patients; respond by fully integrating knowledge about trauma into our practices; and resist re-traumatization. Cognitive-behavioral psychotherapies, such as cognitive processing therapy and narrative exposure therapy, help people challenge and modify unhelpful thoughts and rescript a more adaptive and empowered personal narrative (American Psychological Association, 2017a,b).

CONCLUSION

We may be years away from understanding the polygenic influences on the biology that underlie cognition and emotion and psychiatric disorders in a way that will translate into effective new treatments and preventive interventions (Hyman, 2018); however, we know that the etiology involves interactions between genes and environment that begin before birth and continue throughout life. By using an approach to evaluation and treatment, such as the Perspectives of Psychiatry (McHugh & Slavney, 1998), we develop an impression/formulation of how disease, behavior, personality, and life events interact to contribute to each patient's presentation. Our interventions may include psychopharmacotherapy for the disorder, guidance regarding characteristic ways of responding, and psychotherapies to interrupt maladaptive behaviors and help the patient rescript the life story.

Establishing a therapeutic relationship and guiding change through talking therapies (psychotherapies) is what makes our profession unique among nursing (Smith, 2020). A therapeutic relationship is what helps people feel safe to discuss unusual emotions, thoughts and beliefs, behaviors, and experiences. Without skill in building and maintaining the therapeutic relationship, we are left without the tools we require to gather the history, examine the patient, diagnose, and develop

acceptable person-centered treatments. Keeping up with the science and limitations of psychopharmacological interventions helps us manage our own expectations as well as those of our patients.

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Psychopharmacology

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