DISCUSSION
(6)

Prior to beginning work on this discussion, read the required chapters from the text and review the required articles for this week. Over the course of the past weeks, we have considered the use of medications in the treatment of various psychological disorders. This discussion will provide you with an opportunity to give an informed appraisal on the use of drugs to treat disorders and defend your stance based on your judgment of the literature. In your initial post, describe what you believe are the greatest strengths and weaknesses of using the medications to treat psychological disorders. Evaluate the employment of psychoactive drugs in the treatment of disorders over the lifespan from both an ethical and risk-benefits perspective. Summarize the theories of psychiatric disease and the scientific rationale behind its treatment through the employment of drug therapies. Explain what you believe to be the greatest challenges in the use of psychoactive medications over the next several years. Support your statements with references and logical arguments.

(Article 1)

Problems of Overdiagnosis and Overprescribing in ADHD

By Daniel F. Connor, MD

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ADHD, Attention Deficit Disorders, Child Adolescent Psychiatry

Trends in ADHD diagnosis

ADHD is the most extensively studied pediatric mental health disorder, yet controversy and public debate over the diagnosis and medication treatment of the disorder continue to exist.[1] Questions and concerns are raised by professionals, media commentators, and the public about the possibility of overdiagnosis of ADHD in youths and the possibility of overprescribing stimulant medications. Fueled by sensational media coverage that emphasizes controversy over rationality, the debate can at times become quite heated, leading to a general public assumption that ADHD is overdiagnosed and that stimulant drugs are overused and overprescribed in children and adolescents with and without ADHD.[2]

Trends in ADHD diagnosis and stimulant treatment

ADHD is a psychiatric disorder with a long history. It was first described by the English pediatrician Sir George Frederick Still in 1902, and initial diagnostic classifications emphasized the symptoms of hyperactivity and impulsivity. The diagnostic terms used to describe children with this disorder changed frequently in the 20th century. With the introduction of DSM-III in 1980, the symptom of inattention gained ascendancy and the condition was officially listed as attention-deficit disorder. DSM-IV contains the diagnosis of ADHD with 3 subtypes: combined, inattentive, and hyperactive-impulsive. Further modifications of the criteria for the disorder are expected when DSM-5 is introduced.

Before 1970, the diagnosis of ADHD was relatively rare for schoolchildren and almost nonexistent for adolescents and adults. Between 1980 and 2007, there was an almost 8-fold increase of ADHD prevalence in the United States compared with rates of 40 years ago. Considering the prevalence of school-administered stimulants as synonymous with the prevalence of ADHD, Safer and colleagues[3,4] estimated the prevalence of ADHD in American schoolchildren as 1% in the 1970s, 3% to 5% in the

1980s, and 4% to 5% in the mid to late 1990s. In 2007, using data from the National Survey of Children's Health, Visser and colleagues[5] reported that 7.8% of youths aged 4 to 17 years had a diagnosis of ADHD and 4.3% reported current use of a medication for the disorder.

The rise in prevalence stemmed from a complex confluence of forces and events that came together in the first half of the 1990s and permitted a dramatic expansion of ADHD diagnosis and treatment.[6] The growing political strength of children's welfare advocates and the mental health consumer's movement associated with decreasing stigma resulted in changes to federally funded special education programs. The Individuals with Disabilities Education Act recognized ADHD as a disability, and children with ADHD became eligible for school accommodations.

Beginning in the 1990s, Congress expanded eligibility criteria for Medicaid, especially for children. This fueled a rapid increase in coverage for psychotropic medications, including stimulants.[6] At the same time, scientific knowledge about the longitudinal course of ADHD and its lifetime morbidity, heritability, and neurobiology was rapidly increasing, This provided empiric evidence as well as a scientific and neurobiological rationale for medication intervention.[7,8] Also, the managed care psychiatric carve-out health insurance industry sought to rein in the costs associated with psychiatric illness and supported pharmacological interventions for complex psychiatric disorders, including pediatric disorders.

In 1997, Congress passed the FDA Modernization Act, which encouraged the pharmaceutical industry to develop and test drugs for children by extending patent exclusivity. This resulted in a dramatic increase in randomized controlled trials in children that involved stimulant compounds for ADHD and further supported an evidence-based rationale for medication intervention in ADHD. As a result, the prescribing of stimulants for children with ADHD increased 4-fold between 1987 and 1996, with a further increase of 9.5% between 2000 and 2005. Currently, slightly more than 4% of children and adolescents in the United States use ADHD medications.[5,9]

Doubt and confusion as to where this disorder fits into the general spectrum of illness further feeds the general perception that ADHD is a socially constructed disorder rather than a valid neurobiological disorder.

The rise in stimulant prescribing for youths must be taken in context. Between 1990 and 2005 there was a rapid rise in pediatric prescriptions for many psychiatric medications—not only stimulants. There was a 5-fold increase for antipsychotics between 1993 and 2002, and a 3-fold increase for antidepressants between 1997 and 2002.[10,11] Thus, the rise in stimulant prescribing for pediatric ADHD was only part of a larger shift to an emphasis on medication interventions for the treatment of children with early-onset and complex behavioral and mental health disorders.

Stimulant overprescribing

Public perception of stimulant overprescribing is driven by concerns over the rapid rise in the amount of available stimulants produced in the United States over the past 3 decades. For sale stimulant production quotas are published yearly by the Drug Enforcement Administration.[12] The rapid rise in the production quota of for-sale methylphenidate (excluding amphetamine) is seen in the **Figure**. With the production of more stimulants every year, worries about the increased availability of stimulants for abuse and diversion rise as well. Rising production rates are cited as proof of stimulant overprescribing by physicians and indirect evidence of the overdiagnosis of ADHD among children.[2]

The extant scientific research suggests a much more complicated and nuanced picture of stimulant prescribing. Comparisons of the prevalence of ADHD among youths aged 4 to 17 years (7.8%) with stimulant prescription rates of between 4.3% and 4.4% do not support the idea of a culture of permissive stimulant overprescribing.[5,9] Moreover, recent data from the National Health and Nutrition Examination Survey, a nationally representative probability sample of children aged 8 to 15 years living in the community, indicated an ADHD prevalence rate of 7.8%. However, only 48% of the ADHD sample had received any mental health care over the past 12 months.[13]

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The New York Times

Article 2

OP-ED CONTRIBUTOR

Diagnosis: Human

By Ted Gup

April 2, 2013

THE news that 11 percent of school-age children now receive a diagnosis of attention deficit hyperactivity disorder — some 6.4 million — gave me a chill. My son David was one of those who received that diagnosis.

In his case, he was in the first grade. Indeed, there were psychiatrists who prescribed medication for him even before they met him. One psychiatrist said he would not even see him until he was medicated. For a year I refused to fill the prescription at the pharmacy. Finally, I relented. And so David went on Ritalin, then Adderall, and other drugs that were said to be helpful in combating the condition.

In another age, David might have been called "rambunctious." His battery was a little too large for his body. And so he would leap over the couch, spring to reach the ceiling and show an exuberance for life that came in brilliant microbursts.

As a 21-year-old college senior, he was found on the floor of his room, dead from a fatal mix of alcohol and drugs. The date was Oct. 18, 2011.

No one made him take the heroin and alcohol, and yet I cannot help but hold myself and others to account. I had unknowingly colluded with a system that devalues talking therapy and rushes to medicate, inadvertently sending a message that self-medication, too, is perfectly acceptable.

My son was no angel (though he was to us) and he was known to trade in Adderall, to create a submarket in the drug among his classmates who were themselves all too eager to get their hands on it. What he did cannot be excused, but it should be understood. What he did was to create a market that perfectly mirrored the society in which he grew up, a culture where Big Pharma itself prospers from the off-label uses of drugs, often not tested in children and not approved for the many uses to which they are put.

Keith Negley

And so a generation of students, raised in an environment that encourages medication, are emulating the professionals by using drugs in the classroom as performance enhancers.

And we wonder why it is that they use drugs with such abandon. As all parents learn — at times to their chagrin — our children go to school not only in the classroom but also at home, and the culture they construct for themselves as teenagers and young adults is but a tiny village imitating that to which they were introduced as children.

The issue of permissive drug use and over-diagnosis goes well beyond hyperactivity. In May, the American Psychiatric Association will publish its D.S.M. 5, the Diagnostic and Statistical Manual of Mental Disorders. It is called the bible of the profession. Its latest iteration, like those before, is not merely a window on the profession but on the culture it serves, both reflecting and shaping societal norms. (For instance, until the 1970s, it categorized homosexuality as a mental illness.)

One of the new, more controversial provisions expands depression to include some forms of grief. On its face it makes sense. The grieving often display all the common indicators of depression — loss of interest in life, loss of appetite, irregular sleep patterns, low functionality, etc. But as others have observed, those same symptoms are the very hallmarks of grief itself.

Ours is an age in which the airwaves and media are one large drug emporium that claims to fix everything from sleep to sex. I fear that being human is itself fast becoming a condition. It's as if we are trying to contain grief, and the absolute pain of a loss like mine. We have become increasingly disassociated and estranged from the patterns of life and death, uncomfortable with the messiness of our own humanity, aging and, ultimately, mortality.

Challenge and hardship have become pathologized and monetized. Instead of enhancing our coping skills, we undermine them and seek shortcuts where there are none, eroding the resilience upon which each of us, at some point in our lives, must rely. Diagnosing grief as a part of depression runs the very real risk of delegitimizing that which is most human — the bonds of our love and attachment to one another. The new entry in the D.S.M. cannot tame grief by giving it a name or a subsection, nor render it less frightening or more manageable.

The D.S.M. would do well to recognize that a broken heart is not a medical condition, and that medication is ill-suited to repair some tears. Time does not heal all wounds, closure is a fiction, and so too is the notion that God never asks of us more than we can bear. Enduring the unbearable is sometimes exactly what life asks of us.

But there is a sweetness even to the intensity of this pain I feel. It is the thing that holds me still to my son. And yes, there is a balm even in the pain. I shall let it go when it is time, without reference to the D.S.M., and without the aid of a pill.

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A version of this article appears in print on April 3, 2013, Section A, Page 27 of the New York edition with the headline: Diagnosis: Human

READ 395 COMMENTS

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CHAPTER 17

Challenging Times for Mental Health

In the last edition—the thirteenth—the following paragraph summarized the situation in regard to the psychopharmacological treatment of mental disorders:

> During the last 30 years no new fundamentally novel drugs for mental illness have been developed, and the usefulness of even current medications is being challenged. Efforts to develop an effective drug for Alzheimer's disease have not been successful. Even the criteria by which psychiatric disorders are diagnosed have been revised. Many pharmaceutical companies are abandoning their psychotropic research programs. And all of this is occurring at a time of diminished public resources when the economy has suffered a severe downturn.

Unfortunately, there has not been much progress. There are still no fundamentally new drugs for mental illness or Alzheimer's disease and the benefits of current drug treatment continue to be questioned. Pharmaceutical research into mental illness has not rebounded and although the economy as a whole has gradually recovered, it is not clear if that will be sustained. The need for mental health treatment is still critical, especially for substance use disorders, and particularly for the abuse of opioid prescriptions and "new pharmacological substances." The revision of diagnostic categories has been called inadequate for practical application to real-world difficulties.

These ongoing problems have prompted several responses. First, the limitations of traditional psychopharmacological treatment have reactivated interest and support for nonpharmacological approaches to mental illness, particularly psychotherapy, but also somatic treatments, such as transcranial therapy for depression. Second, the scope of pharmacological research is being extended to include a deeper understanding of basic neurophysiology, such as the circuitry of fear, rather than specific clinical syndromes, such as anxiety symptoms. Third, there

EPIDEMIOLOGY OF MENTAL ILLNESS

According to Substance Abuse and Mental Health Services Administration's (2016; SAMHSA) National Survey on Drug Use and Health (NSDUH), an estimated 43.4 million (17.9 percent) of Americans ages 18 and up experienced some form of mental illness in 2015. In 2015, over 27 million people in the United States reported current use of illicit drugs or misuse of prescription drugs and over 66 million people—nearly a *quarter of the adult and adolescent population*—reported binge drinking in the past month. Among these, 7.9 million people had both a mental disorder and substance use disorder, that is, a co-occurring mental *and* substance use disorder.

Serious mental illness (SMI), defined by the SAMHSA as resulting in serious functional impairment, affects nearly 10 million American adults each year. According to the National Survey on Drug Use and Health (NSDUH), in 2015, there were an estimated 9.8 million adults aged 18 or older in the United States with SMI within the past year. This number represented 4.0 percent of all U.S. adults.

Consistent with previous reports, Walker and colleagues (2015) summarized data from 148 studies and found that individuals suffering from mental illness had a relative risk of mortality that was 2.22 times higher than the comparison population. Furthermore, they estimate that about 8 million deaths were related to mental disorders every year with a potential median of a decade of lost life. The likelihood of homicide was more than seven times greater among those with any mental disorder than in the general population, according to one analysis (Crump et al., 2013), and for those with substance abuse disorders, the risk was 16 times greater. People with mental illness are also four times more likely to be victimized in nonlethal violent incidents than people in the general population.

How does this situation compare with previous estimates? It has been proposed that we are in the middle of a mental health crisis. The number of psychiatric beds in state hospitals has dropped to a historic low from 558,922 in 1955 (337 per 100,000) to 37,679 in 2016 (11.7 per 100,000) (Fuller et al., 2016). Between 2003 and 2013, there was a 10.2 percent decrease in the number of psychiatrists per 100,000 people in

surveyed locations. During the same time, there was an increase in the numbers of primary care physicians and neurologists (Bishop et al., 2016). The decline in psychiatrists has been attributed to poor reimbursement, lack of coverage (such as when psychiatric diagnoses are not considered a "medical" condition), or problems qualifying for disability.

The existence of an epidemic in mental illness has also been refuted (Pies, 2015). First, it has been argued that the increase in the incidence and prevalence of mental disorders was not estimated correctly because these values were calculated from rates of medication prescriptions, diagnoses and treatment rates made in offices, or "putative" assessments of disability assumed to be due to mental illness. These indirect measures are not synonymous with a true increase in prevalence. Second, epidemiological surveys found that in 2013, the rate of SMI in U.S. adults was 4.2, while in 2010 the number was 5.0 and in 2009, 4.8 percent. The SMI rate was estimated at 8.3 percent in 2002 and 5.4 percent in 1990. Although estimates may vary, depending on the data source, the demographic data do not show a current epidemic of serious mental illness. Similar outcomes are seen in specific disorders with no evidence of significant increases in the proportion of adults with depression or schizophrenia. This is also true for children and adolescents with SMI.

Nevertheless, a substantial number of individuals continue to suffer from the burden of mental health disorders. The World Health Organization estimates that one in four people will have an episode of mental illness in their lifetime, and that mental and behavioral problems are the biggest single cause of disability on the planet (World Health Organization, 2001). Unfortunately, most people with behavioral problems do not receive therapy. Surveys report that as few as 35 percent of people with severe symptoms of depression were seen by a mental health therapist in the past year (Pratt and Brody, 2014). A survey by SAMHSA found that the reasons people gave for not seeking care included the expense, not having mental health insurance, the stigma of a mental illness diagnosis, fear of losing a job, and privacy concerns. Such views inhibit people from getting help. In one study, 93 percent of individuals with schizophrenia, depression, or bipolar disorder anticipated discrimination—and 87 percent experienced it—in at least one area of life, such as in their social life, education, housing, work, and so on (Farrelly et al., 2014). This perspective seems consistent with results of a global survey about mental illness in which responses were obtained from more than 1 million people and 229 sites. While nearly half of those surveyed from developed nations believed that mental illness and physical illness were similar, only 7 percent of this same group felt that mental illness could be overcome (Seeman et al., 2016).

Unfortunately, there have been no significant improvements in the pharmacological treatment of mental disorders. After the development of Prozac and the newer antipsychotic drugs decades ago, psychiatric researchers attempted to maintain these successes and to address the stigmatization of the mentally ill by focusing on the medical model, that is, by emphasizing that mental illness is a brain disease (Makari, 2015). But the newest drugs, while safer and with fewer side effects, target the same transmitter systems as the older ones and do not improve outcomes (Friedman, 2015). Acknowledgement of this situation prompted a reassessment of the approach to diagnosis, research, and treatment of mental illness.

Diagnostic Revisions

Publication of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) in May 2013 was a significant development in the mental health profession. In general, there was an overall effort to improve what is known about the relationship between behavioral and psychological disorders—as well as their relationships to conditions covered by other applicable medical specialties—and move toward a more global system. Another important change was that the new manual was more compatible with the *International Classification of Diseases* (ICD) *System*, which is used by the rest of the world outside of North America. That is, the revisions of the DSM-5 are now more aligned with the structure of the disorders in the ICD (Clay, 2013). A third difference is the use of a continuum of symptoms rather than discrete diagnostic boundaries. Fourth, the "multiaxial" system, which used five different axes for psychiatric diagnoses, comorbid medical conditions, nonmedical factors, and other disabilities, was discontinued. In general, intellectual and personality disorders were given more equality with other diagnoses (Kupfer et al., 2013).

Research Domain Criteria: A Research Framework for New Ways of Studying Mental Disorders

The current diagnostic system of the DSM tried to apply a scientific basis for the distinction between those who were sick and those who were well. But the National

Institute for Mental Health recently rejected this approach and stated that it was not producing useful research (Luhrmann, 2015). In 2013, its director, Thomas R. Insel, stated that no unique neurophysiological processes had been discovered by psychiatric research that could explain specific diagnoses. The DSM criteria had not kept up with developments in genetics, neuroscience, and behavioral science. The system for reviewing research grant applications had been based on DSM-defined disorders, but researchers increasingly wanted to study certain mechanisms, such as working memory, that cut across disorders.

Research into the neurobiology of mental disorders showed similar neuronal substrates across diagnostic categories. It was concluded that diagnoses were not useful or accurate for understanding the brain and would no longer be used to guide research. The institute eliminated the tradition in which research was guided by diagnoses, for example, a scientist who would identify as a "depression" researcher.

A new program was developed called *Research Domain Criteria* (RDoC). Under this scheme, all research protocols must have a neuroscientific basis in some biological structure, such as genes, cells, or circuits, that cuts across behavioral, cognitive, and social domains, such as acute fear, loss, or arousal. Since 2014, in order to receive the institute's support, clinical researchers must explicitly focus on a target such as a biomarker or neural circuit. To use an example from the program's Web site, psychiatric researchers will no longer study people with anxiety; instead they will study *fear circuitry*.

The RDoC is not a new distinct diagnostic nosology, but rather a research paradigm about psychopathology intended to build a research literature based on genetics, neuroscience, and behavioral science (Cuthbert, 2014). It is a four-dimensional matrix. The first dimension is divided into five major domains of functioning. They include:

1. Aversive properties, that is, those systems that respond to aversive or negative situations
2. Appetitive properties, or a "positive valence," such as working toward rewards
3. Cognitive systems
4. Systems for social processes
5. Arousal and regulatory systems

The second dimension includes what are called "units of analysis." These are different ways in which one can study the functional domains of the first dimension.

They include genetics; molecular processes and cellular processes; measures of circuits; physiological measures, such as heart rate, skin conductance, or serum cortisol; behavioral measures, such as an assessment battery; and self-reports, which are defined to include questionnaires as well as structured diagnostic interviews. The aim is to acquire a comprehensive understanding of how a particular concept, such as "working memory," works at multiple levels.

The third dimension is neurodevelopment. This is important because psychiatric disorders are now understood to be developmental disorders. Therefore, it is vital to understand how the functional domains and the units of analysis described earlier evolve with the maturing organism.

The fourth dimension is environmental influences. When something happens in the environment at a certain stage of neurodevelopment, it can influence the functioning of all of the above dimensions. Over all, the emphasis is on broader research to identify etiology and find better targets.

Resurgence of Nonpharmacological Therapies

Neurobiological mechanisms mediate all of our human experience, and it is certainly worthwhile to learn as much as possible about how the brain works. But that is not the same as assuming that our experiences of low mood or psychosis, for example, should be labeled as an illness. It is being increasingly appreciated that even severe mental disorders are not simply due to genetic anomalies or impaired brain substrates. The role of experience is being realized as an important contribution to our mental state, and that even severe mental problems may be the result of traumatic life events that alter our interaction with the world. The ultimate benefit of psychiatric medications is being questioned, relative to that of psychological and behavioral therapies (Kinderman, 2014).

This is illustrated by a study by Leucht and colleagues, who performed a meta-analytical review of the effectiveness of medication and psychotherapy for major psychiatric conditions (see Huhn et al., 2014). They organized 61 meta-analyses on 21 disorders, which included 137,126 patients, into 3 comparisons: pharmacotherapy (33 meta-analyses) or psychotherapy (17 meta-analyses) compared with placebo or no treatment; head-to-head comparisons of pharmaco- and psychotherapies (7

meta-analyses); and combinations of both treatments (12 meta-analyses). Direct comparisons showed that psychotherapy had a slight edge in regard to preventing a relapse into depression and bulimia; pharmacotherapy was more effective for dysthymic disorder and schizophrenia. Therapeutic combinations were more effective than either therapy alone, except for posttraumatic stress disorder and psychodynamic therapy for schizophrenia.

Although pills are cheaper and faster, it is not uncommon for patients to prefer psychotherapy. In their meta-analysis of the literature, McHugh and coworkers (2013) provided an estimate of the proportion of patients that preferred psychotherapeutic approaches as opposed to medications for treatment of psychiatric disorders. Overall, they reported a "threefold preference for psychological treatment relative to medication" (p. 595). This was most evident in younger patients and in women. Moreover, many problems are social and environmental, for which there is no quick biological cure. Furthermore, some disorders, such as borderline and narcissistic personality disorders, are known not to have drug treatments, but can respond to therapy (Friedman, 2015). See discussion by Boggs, 2014.

Davey (2014) expressed this perspective as a summary of the shortcomings of (current) drug treatments for mental illness, which include:

1. Drugs alone are not good enough, may promote relapse, and are more effective when combined with psychotherapy.
2. Drugs may unnecessarily turn a short-term problem into a lifetime concern.
3. Drugs may give the message that mental problems are purely a medical issue and "out of the hands" of the patient.
4. Diagnostic criteria are all or none, not dimensional; but symptoms may vary in intensity.
5. Drugs are being promoted for normal difficulties of life.
6. Side effects of drugs, especially psychological, may cause people to stop taking them or diminish their benefit.
7. There are publication biases for reporting the positive effects of drugs.
8. Drugs do not help change the way people think or their socioeconomic environments.
9. Poorly trained practitioners make it easier to use drugs.
10. Drug companies have more clout than psychotherapy groups.

On the other hand, the alternative of psychotherapy is not always available; it may not be covered by insurance; it can be expensive; and it may take much longer

to be effective than some drug treatments, for example, to alleviate anxiety. Nevertheless, many medications, such as drugs for the treatment of psychosis and bipolar disorder, may take weeks to show improvement, and it may take more than one trial to determine the optimum dose regimen. During that time, psychological support is, understandably, crucial to maintain the best outcome for the patient. Unfortunately, the overall success rate of psychiatric medications has remained relatively constant at only about 66 percent.

Policy Developments

In December 2016, President Barack Obama signed the 21st Century Cures Act after it sailed through the House of Representatives and was passed by the Senate 94 to 5. Although the Act has been acclaimed for its provisions to accelerate drug discovery, it also contains sections meant to improve mental health treatment and to fight the opioid epidemic. Continued support for the latter objective was provided when President Trump declared the opioid epidemic a "national public health emergency" in October 2017. Supporters have proposed that it is the most important piece of legislation concerning mental health since the 2008 law requiring parity of insurance coverage for mental and physical health.

There is strong support for science in this new legislation. Federal agencies are urged to fund only those initiatives with significant research backing and to determine if patients truly benefit. Laws that mandated parity for mental and physical therapies are strengthened. Furthermore, there are provisions for increasing the number of psychiatrists and psychologists to alleviate the current shortage.

In addition, the law synthesizes ideas from several legislators and urges the states to offer early intervention for psychosis, an approach that is considered to have great potential for improving mental health.

The bill was crafted with input from many stakeholders, including patients, researchers, and industry representatives. Most provisions are noncontroversial, such as proposals for a strategic plan, initiatives for specific research efforts, sharing of data, and promoting reproducibility of research outcomes. Billions of dollars are designated for individual projects, such as Vice President Biden's cancer

"moonshot," and $30 million are earmarked for regenerative medicine research using adult stem cells.

Clinical Examples

The following examples illustrate clinical applications of current understanding of best practices in psychopharmacology. Clients L (Thomas et al., 2012), M (Ostermann et al., 2013), and N (Doellinger et al., 2016) are taken from the clinical literature and describe real-life case presentations.[1]

Client A was a 45-year-old male who was prescribed lithium for a diagnosis of bipolar II disorder. He presented with complaints of an 80-pound weight gain and an inability to remember names. Recognizing these problems as side effects of lithium therapy, the therapists noted a study on the efficacy of valproic acid for bipolar II and decided to make that medication switch. Thereafter, Client A lost about 40 pounds and his memory function improved, allowing him to continue working.

Five years later, Client A presented with complaints of listlessness, lack of energy, and sexual dysfunction. It was discovered that the client had been diagnosed with depression and had been prescribed *escitalopram* (Lexapro) in addition to the valproic acid. Escitalopram and valproic acid were discontinued and the initiation of *aripiprazole* (Abilify) and *lamotrigine* (Lamictal) was recommended, either alone or in combination. Valproic acid and escitalopram were replaced with aripiprazole. Two weeks later, the client reported that the new drug was "intolerable" and complained of aches, myalgias, flulike symptoms, and electric shocks in his head. The psychologist determined that the client had serotonin discontinuation syndrome rather than side effects of aripiprazole and counseled the client about serotonin discontinuation syndrome. Three weeks later, the symptoms had ceased, the client was more energized, sexual function was improving, and no bipolar symptoms were reported. Continual progress was made over the next few months.

Client B, a man in his late twenties, was referred by a physician for evaluation of cognitive difficulties. Neuropsychological testing was performed and diagnosis was made of notable cognitive dysfunction, with the greatest difficulty being word finding. Medication review revealed that the client had recently been prescribed *topiramate* (Topamax) for anxiety and posttraumatic stress disorder (PTSD).

Replacement of the topiramate with *pregabalin* (Lyrica) led to rapid resolution of the cognitive difficulties.

Client C was a 48-year-old woman diagnosed with depression and anxiety. She was prescribed *sertraline* (Zoloft) and showed some improvement, but she gradually developed a panic disorder. Further history taking revealed that she had recently undergone surgery for breast lesions that were diagnosed as benign breast cysts. It turned out that Client C was a heavy coffee drinker. Sertraline interferes with the metabolism of caffeine, which resulted doubling her blood level of caffeine. Caffeinism is associated with increasing anxiety, panic disorder, and the development of benign breast cysts. Cessation of caffeine drinking, which included drinking smaller amounts of caffeinated and eventually only drinking decaffeinated coffee, led to resolution of the panic disorder.

Client D was a 28-year-old Gulf War veteran with severe PTSD, presenting with nighttime terrors and threatening actions toward his wife. Moreover, he was amnestic for these episodes. Medication review revealed a prescription for *zolpidem* (Ambien) for sleep. It was determined that the Ambien might be causing the amnesia. Replacement of Ambien with gabapentin at bedtime improved PTSD symptoms and the amnestic episodes were resolved.

Client E was an 88-year-old female care center resident whose family took her to therapy for increasing dementia. Medication review revealed that she had been receiving *imipramine* (Tofranil) for depression and *diazepam* (Valium) for anxiety and sleep difficulties. Because tricyclic antidepressants have anticholinergic difficulties, they can cause cognitive impairments. Benzodiazepines are widely known to worsen dementias. Cessation of these medicines and replacement with *quetiapine* (Seroquel) and *mirtazapine* (Remeron) at bedtime led to cognitive improvements, reductions in anxiety, better sleep patterns, and improvements in appetite.

Client F was a 5-year-old girl presenting with rages and aggressive behaviors made worse by psychostimulants and antidepressants. She was prescribed *valproic acid* (Depakote) and showed marked improvement in behavior. When she was referred to a psychologist, it was decided that with behavioral improvement, family therapy could be instituted to address problems underlying the client's behaviors. The possibility was also raised that, with effective family therapy, the valproic acid might eventually be stopped.

Client G, a 69-year-old female, was brought to the emergency department confused and disoriented—she did not know where she was—and suffering from delusions—stating that she was a movie star and the hospital a movie studio. She experienced a fluctuating course of agitation, had not slept in days, and was aggressive and disruptive. She had no history of mental illness and there was no evidence of illegal drug or alcohol use. The medical examination revealed a systemic infection; laboratory tests also indicated an elevation in her serum glucose levels. The psychologist determined that the patient was in a state of delirium possibly caused by her systemic infection. The goal was to stabilize her behaviorally and to treat the source of the infection. It was important to reduce her level of agitation, provide treatment for her delusion, improve her orientation, and provide something that allowed her to sleep.

The recommendation was to use the second-generation antipsychotic drug risperidone rather than the alternate option of a benzodiazepine, because in elderly patients and those with delirium, a benzodiazepine has the potential to paradoxically increase agitation and worsen the delirium, an idiosyncratic response. There was a need for an antipsychotic that could be given by intramuscular injection to reduce the agitation quickly and facilitate sleep. Afterwards, the drug could be given orally on a regular dosing schedule to maintain stability. Several antipsychotics have acute intramuscular formulations, including haloperidol, risperidone, olanzapine, and aripiprazole. Haloperidol was excluded because of the concern for producing extrapyramidal side effects, which are more likely in the elderly, and when the drug is given by intramuscular injection. The hospital formulary did not include aripiprazole; olanzapine was excluded because its high anticholinergic effect would tend to worsen the delirium. In addition, olanzapine has a risk of producing metabolic side effects that include insulin resistance and can worsen diabetes. Since this patient had increased blood glucose levels, olanzapine would not be the best choice. It was felt that risperidone was the least risky and would provide the most benefit. Risperidone was given in small doses, that is, 0.5 milligram via intramuscular injection on an as-needed basis and then orally in low doses, starting with 0.5 milligram twice per day. With this regimen, the patient was able to sleep, her delusion subsided, and she became calm and regained her orientation to place. She was able to be discharged after two days with a referral to an outpatient psychiatrist who could follow her for ongoing treatment as needed.

Client H was a 55-year-old diabetic man with mild hypertension and painful

inhibitors. Given his mild hypertension, venlafaxine was not chosen. Although tricyclic antidepressants can help with neuropathic pain and depression, they are not a good choice, given their side effect profile and lethality in overdose. Duloxetine has an indication for neuropathic pain, depression, and anxiety, and was successfully prescribed. Because duloxetine is a CYP2D6 and CPY1A2 inhibitor and has potential drug–drug interactions, the patient was instructed to tell his physician if he took any other medications or supplements.

Client I was a 33-year-old woman hospitalized with her first episode of mania. She had no previous history of a depressive episode, no drug or alcohol history, and no medical issues. Because her first presentation was a manic episode, she was prescribed lithium. Prior to starting that drug, however, she was given a pregnancy test, and her baseline serum creatinine and thyroid hormone levels were obtained. Her choice of a birth control method was discussed and documented. She was prescribed the average starting dose of 300 milligrams twice a day, but after one week, she complained of stomach irritation and some diarrhea. Because gastrointestinal irritation and diarrhea are common, particularly early in treatment, she was encouraged to drink adequate fluid. Then the dose of 300 milligrams twice a day was maintained to see if the side effects resolved.

Client J was a 27-year-old male admitted secondary to a manic episode. He had five to six manic or depressive episodes a year and struggled on and off with alcohol abuse. Valproic acid treatment was started because the patient was a rapid cycler, with four or more depressive or manic episodes per year, and because of his comorbid alcohol abuse. He started on 250 milligrams twice a day, which was increased to 500 milligrams twice a day. His valproic acid blood level was low and it turned out that his liver enzymes had doubled. While it is not unusual for patients on anticonvulsants to experience an increase in liver enzymes, as long as their dosage is not tripled, no change in therapy is indicated. Nevertheless, the patient should be monitored.

Client K, a 21-year-old male with symptoms consistent with schizophrenia, was admitted because of profound psychotic behavior. He was treatment naive and an antipsychotic was recommended. His fasting lipid profile showed that the patient had mildly elevated total cholesterol and a low HDL—a so-called good cholesterol—for his age. Because of the increased risk of dyslipidemia, olanzapine and quetiapine were ruled out, and risperidone, ziprasidone, and aripiprazole were recommended. But when risperidone was started and increased to 3 milligrams

twice a day, which is a high average dose, the patient complained that he felt "uncomfortable" in his skin, like "I can't sit still." Given his descriptions, he was likely experiencing akathisia, which is not uncommon with risperidone. Because akathisia is associated with an increased risk for suicide, it needs to be addressed, although current options are often unsatisfactory. For client K, the dose of risperidone was reduced, but then the psychosis worsened. A low, 15-milligram dose of the 5HT2 serotoninergic antagonist mirtazapine was added and the patient's akathisia decreased. The goal was to eventually reduce the risperidone dose so that the adjunct mirtazapine would effectively suppress the akathisia.

Client L was a 20-year-old unmarried healthy male without a previous psychiatric diagnosis or therapy. He was brought to the emergency department by police in a condition of acute agitation, confusion, suicidal thoughts, and self-inflicted injury as a result of smoking the synthetic cannabinoid drug, K2. The symptoms were consistent with known psychiatric effects of K2. In addition to the agitation and significant abrasions, the patient's respiratory rate was 30. After the patient was stabilized, he was transferred for monitoring to the inpatient psychiatric unit. The next day, the psychiatric evaluation concluded that there was complete resolution of his symptoms. The patient was discharged to his home, as he maintained his denial of any prior psychiatric history.

Client M was a 49-year-old male admitted with a diagnosis of a first-time severe, major depression as a result of discontinuation of 8 years of daily triptan use. Triptans are indicated for acute migraine treatment. Their mechanisms of action include high-affinity serotonin 5-HT(1B/D) receptor agonism with less potent 5-HT(1A) receptor affinity. Major depression has been reported to occur as a result of both migraine headaches as well as triptan administration. Previous treatment with serotonergic antidepressants were ineffective for client M. His depressive symptoms, however, were successfully resolved with a nonserotonergic medication. This is the first demonstration that abrupt termination of chronic extensive triptan use may elicit severe major depression. The symptoms were most likely be due to long-term serotonergic changes, such as downregulation and desensitization of 5-HT(1) receptors. The current case suggests that nonserotonergic medications may be a useful alternative for this condition.

Client N, a 53-year-old woman diagnosed with recurrent major depression, was admitted to the psychiatry department suffering from a severe depressive episode lasting six weeks, which was accompanied by psychotic symptoms. Her current medications were 200 milligrams of sertraline per day and 2 milligrams of

risperidone per day. For eight weeks, she was treated with the same sertraline dose, 4 milligrams of risperidone and slow-release bupropion titrated to 300 milligrams per day. When this regimen did not produce any improvement, a course of eight to ten electroconvulsive therapy (ECT) sessions were started. Two days after the first session, the patient had 3 generalized tonic–clonic seizures within 6 hours. After phenytoin and valproic acid were added to the daily medications, there were no more seizures. Two days later, following clinical consultation, phenytoin and bupropion were withdrawn and ECT resumed. There were no more seizures, and the patient was eventually discharged after substantial improvement and recovery from depressive symptoms. This case describes the occurrence of post-ECT spontaneous seizures that might have been induced by the addition of bupropion, which can have proconvulsive effects, although convulsive thresholds may also be reduced by both sertraline and risperidone.

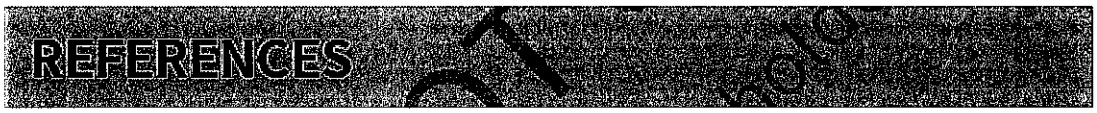
What do these cases have in common? First, all clients had been prescribed reasonable medications as therapy. Second, while efficacious, all the medications had significant side effects that limited optimal life functioning. Third, suggestions were made for reasonable modifications in therapy that often resulted in improved compliance, better life functioning, or amenability to the institution of psychological therapies.

To make specific suggestions for a client, it is important to be aware of three important factors that may affect patient compliance:

1. *Can the client afford the prescribed medication?* Patients and physicians alike are susceptible to ads for heavily promoted, expensive, brand-name medications. New medicines may have significant advantages over older medicines, but they also have their own constellation of side effects. Fortunately, in the past couple of years, numerous psychotherapeutic drugs have become available in less-expensive generic forms.
2. *Can the client tolerate any degree of weight gain?* Some clients can tolerate a degree of weight gain, while undesirable weight gain might lead to noncompliance in others. In choosing an antidepressant, for example, *mirtazapine* (Remeron) might be appropriate for a client who can tolerate weight gain, while *duloxetine* (Cymbalta) or *bupropion* (Wellbutrin) might be appropriate for a client who wants to lose weight. The same considerations apply in the treatment of bipolar disorder and behavioral disorders associated with anger, agitation, and aggressive behaviors.
3. *Can the client tolerate any degree of cognitive dysfunction?* Many psychotherapeutic drugs are associated with drug-induced cognitive

STUDY QUESTIONS

1. For the past two decades, there have been few new pharmacological treatments for mental illnesses. What other therapies or approaches to the treatment of mental disorders have been reexamined as a result?
2. What are the major revisions of the ***Diagnostic and Statistical Manual of Mental Disorders*** (DSM-5)?
3. What are the Research Domain Criteria and why were they developed?
4. What are some of the major shortcomings of current pharmacological treatment for mental illness?
5. What are the main proposals of the 21st Century Cures Act?
6. Do you find any of the case studies particularly relevant and if so, why? What are the three most important factors in regard to patient compliance with drug therapy? Do you have any vignettes you might add?



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