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Developments in Neuropsychiatric Treatment

New Challenges and Old Problems

Paul C. McCabe and Steven R. Shaw

INTRODUCTION

Advances in medical science have enabled researchers to study brain-behavior connections with greater specificity than ever before. While there has always been a presumed connection between biological mechanisms and behavior, affect, and personality, limitations in medical science restricted this association to the hypothetical at best. However, new technologies employed to study the ways that neural mechanisms interrelate, and new understandings about the neurochemical patterns leading to disordered behavior, have helped to advance diagnostic and treatment accuracy of psychiatric conditions. For example, advances in research focused on neuronal integration, which is the coordination and adjustment of neural activity across multiple brain regions, have helped develop models that explain how complex behavior, such as emotion and cognition, occur (Northoff, 2008). These advances have helped elucidate the neuropsychiatric foundations of behavior, emotion, personality, as well as the origin and prolongation of disordered behavior.

Despite these advances, there remain challenges in the treatment of psychiatric conditions. Our understanding of the structure and function of

neuronal integrated networks is increasingly advanced, but there remain questions with regard to mechanisms of interneuronal communication. The precise nature of how neurotransmitters are fitted to adjoining neurons either to facilitate or block a transmission is not entirely understood. Yet psychopharmacological medications are manufactured with the intention of facilitating or impeding this interneuronal exchange. Newer medications can increasingly target precise neural systems through enhanced specificity, but side effects remain a problem and impact treatment adherence. Although science has facilitated a greater understanding of the neurological bases of psychiatric disorders, most medications designed to ameliorate these disorders cannot be solely used as a panacea. Rather, most neuropsychiatric conditions require a balance of psychopharmacology and psychotherapeutic intervention for optimal results. Educators are cautioned that while advances in neuropsychiatric science are encouraging, a multipronged multidisciplinary approach is likely the best strategy to identify and treat psychiatric conditions.

LINKING NEUROTRANSMITTERS TO BEHAVIOR

Recent research has identified specific neurotransmitters and receptor sites implicated in a variety of functions associated with cognition, emotion, and behavior. For example, while research has confirmed the role of the neurotransmitter serotonin as participatory in cognitive tasks, more recent research has identified serotonin subtypes responsible for supporting specific higher-order functions. The serotonin subtype 5-HT_{1A} has been identified as having a primary role in coordinating memory consolidation, and stimulation of 5-HT_{1A} receptors in rats has led to learning impairments by inhibiting memory-encoding mechanisms (Ögren et al., 2008). The receptor has also been implicated in the retrieval of aversive or emotional memories, suggesting a primary role in memory consolidation tasks (Ögren et al.). In addition, 5-HT_{1A} has been associated with a number of psychiatric disorders, including depression, panic disorder, and neurosis—all of which have symptoms that include or are triggered by emotionally laden memories. Furthermore, specific alleles located on the 5-HT_{1A} gene [e.g., C(-1019)] have been identified as playing a functional role in 5-HT_{1A} receptor irregularities and predisposition to mental illness (François, Czesak, Steubl, & Albert, 2008).

Similarly, recent research has identified multiple receptor sites for the neurotransmitter dopamine, which is implicated in dopaminergic functions. Dopamine plays a role in a variety of behaviors and cognitive functions, including attention, arousal, mood, learning, and more. It has also been associated with operation of the reward and motivation centers of the brain. The interrelationships among neurotransmitters is complex. For example, dopamine is a precursor for other neurotransmitters, including norepinephrine and epinephrine, and dopamine has a complementary or reciprocal relationship with neurotransmitters such as glutamate and GABA. Researchers are continuing to investigate these complex relationships in facilitating or inhibiting a variety of neural functions.

INCREASING SPECIFICITY OF MEDICATIONS

Medications that bind to specific receptors rather than impacting multiple neurotransmitter systems have greatly improved the efficacy of psychopharmacological interventions while reducing side effects. For example, older classes of antipsychotic medications affect multiple dopaminergic receptors by reducing the amount of available dopamine at the synapse, thus blocking dopamine transmissions and consequently reducing psychotic symptoms. However, other behavioral systems are also interrupted in the process, such as physical motor coordination, which can lead to Parkinsonian-like motor responses. As noted above, reducing the amount of available dopamine would also reduce the amount of successor neurotransmitters such as norepinephrine, which has an important role in modulating emotions, stress, and attention.

However, medications that target specific dopamine receptors (e.g., dopamine 2, or D2), such as partial dopamine agonists used in treating symptoms of schizophrenia, have been helpful in reducing powerful side effects that affect arousal, attention, motor functions, and so on. These newer classes of partial dopamine antagonists have shown promise with children and adolescents with schizophrenia by reducing positive and negative symptoms of the disorder (Findling et al., 2008). Other researchers pursuing competing neural pathways, such as regulating and inhibiting the neurotransmitter glutamate as a means to reduce psychotic symptoms, are finding promising results (Paz, Tardito, Atzori, & Tseng, 2008). This is important, as new evidence is suggesting that prolonged exposure to anti-dopaminergic medications, including those specifically targeting D2 subtype receptors, may lead to cortical atrophy (Paz et al.) and inhibit the growth of new synaptic connections within the dopamine system (Fasano, DesGroseillers, & Trudeau, 2008).

Increasing specificity of medications and the invention of medications affecting differing neurotransmitter systems is helping medical professionals tailor interventions to the precise symptoms associated with a particular psychopathology. For example, treatments for depression now include a variety of medications that target different neurotransmitter systems. This newer class of medications includes selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), norepinephrine and dopamine reuptake inhibitors (NDRIs), and noradrenergic and specific serotonergic antidepressants (NaSSAs). There are more in development, including a triple-action serotonin-noradrenaline-dopamine reuptake inhibitor (SNDRI) that is showing early promise as an antidepressant (Breuer et al., 2008) as well as an anti-obesity agent (Tizzano et al., 2008). These medications have the potential to target multiple problems associated with complex psychiatric conditions.

MEDICATION SIDE EFFECTS

Despite advances in medication therapies, side effects caused by treatment regimens remain significant obstacles. The greater the medication side effects, the more likely treatment adherence will be affected. However,

when medication specificity increases affinity to target receptor subtypes (rather than global receptor systems) and lowers affinity to undesired receptor subtypes, the result is a diminution of the pervasiveness and intensity of unwanted side effects (Tallman & Dahl, 2002).

Common side effects for the newer classes of antidepressant medications include insomnia, restlessness, anxiety, nausea, weight gain or loss, sweating, dry mouth, drowsiness, diarrhea, and headaches. These effects can range from mild to severe in intensity and frequency. The newer antipsychotic medications include side effects such as drowsiness, tachycardia (increased heart rate), dizziness, weight gain, reduced sexual arousal or interest, rash, tremor, problems with menstrual cycle, and extrapyramidal motor effects (National Institute of Mental Health, 2008). The degree to which children and adolescents can cope with medication effects and understand how the medications are helping them will determine whether or not they will adhere to the regimen.

Most psychopharmacological drugs, including newer medications, generate unwanted side effects. However, the newer medications generally produce fewer and less intense effects that are more easily tolerated. Children and adolescents are particularly susceptible to any medication effects that make them feel or appear abnormal or cause significant physical distress. It is important that physicians, parents, and the school multidisciplinary team work with students to help them understand the purpose of the medications and any anticipated side effects.

(DE-)EMPHASIS ON TALK THERAPIES

The changing landscape of medical insurance provision has been cited as one of the primary reasons behind the increased prescription of psychopharmacological drugs and concomitant decrease in psychotherapies used to treat neuropsychiatric conditions. Between 1996 and 2005, the number of office visits to psychiatrists decreased from 44.4% to 28.9%, and the percentage of psychiatrists who provide psychotherapy to their patients dropped from 19.1% to 10.8% (Mojtabai & Olfson, 2008). Meanwhile, the prescription rates for psychopharmacological prescriptions increased during the same period. This trend can be attributed to growth and advancement of psychopharmacological treatments, but it is also likely a by-product of financial incentives brought about by changes in reimbursement through managed care (Mojtabai & Olfson).

Despite this trend, research on most forms of psychopathology indicates that psychotherapeutic interventions contribute significantly to treatment gains and, in some cases, are superior to psychopharmacology. A meta-analysis of treatments for depression indicated that both psychotherapy and medication are effective treatments; however, psychotherapy provides a prophylactic effect that medication does not (Imel, Malterer, McKay, & Wampold, 2008), and this positive effect is evident up to 6 months later (David, Szentagotai, Lupu, & Cosman, 2008). For many disorders, a combined approach of psychopharmacological intervention plus cognitive-behavioral therapy demonstrates the most favorable outcome; these include body dysmorphic disorder (Ipser, Sander, & Stein, 2009), obsessive-compulsive

disorder (Flament, Geller, Irak, & Blier, 2007), and attention deficit/hyperactivity disorder (ADHD; Bachmann, Bachmann, Rief, & Matthejat, 2008). The superiority of psychotherapy over psychopharmacology for treatment efficacy has been well demonstrated in meta-analytic studies of child and adolescent conduct disorder, depressive disorders, and anxiety disorders (Bachmann et al.).

Furthermore, recent studies are questioning whether some psychopharmacological treatments are even effective beyond the placebo effect. Kirsch et al. (2008) evaluated the adult medication trials for four SSRI antidepressants (fluoxetine [e.g., Prozac], venlafaxine [e.g., Effexor], nefazodone [e.g., Serzone], and paroxetine [e.g., Paxil]) that were submitted to the Food and Drug Administration between 1987 and 1999. They found that the greater the symptom severity, the more likely the medications demonstrated efficacy; however, treatment effect sizes were relatively small even for severely depressed patients (Kirsch et al.). Similar results have been found in reviews of research on children and adolescents treated with antidepressants. In one review, the authors concluded that "in general, nine depressed youth must be treated with an antidepressant to obtain one clinical response above that achieved with placebo" (Boylan, Romero, & Birmaher, 2007, p. 27). They further reported that between 1 and 3 children out of 100 taking antidepressants showed onset or worsening of suicidality and, therefore, recommended the use of antidepressants in only the most severe cases.

FUTURE DIRECTIONS

Despite advances in neuropsychiatric science and psychopharmacological specificity, significant challenges remain regarding the use of these treatments with children and adolescents. There is a significant paucity of clinical trials of most psychopharmacological medications with these age groups. Therefore, an insufficient database exists regarding efficacy, safety, adverse events, and long-term outcomes for children and adolescents (Koelch, Schnoor, & Fegert, 2008), and this information cannot be reliably extrapolated from adult trials (Vitiello, 2003). Clearly, one must consider ethical concerns when organizing clinical trials of psychopharmacological medications with children and adolescents. Scholars have advocated for integration of research ethics into the research development and design as opposed to applying research ethics from an oversight perspective (Tan & Koelch, 2008). Much additional research on the efficacy and safety of child and adolescent psychopharmacology still needs to be done.

In the meantime, we already know that many psychotherapy protocols have been empirically validated with a range of psychiatric conditions and can be successfully implicated without concern for adverse effects. Research has unequivocally demonstrated that the use of psychopharmacological agents alone as the sole means of treatment is rarely effective and that it fails to inoculate the individual against future occurrences (thus promoting dependence on the medication). Psychological and psychosocial interventions addressing children's emotional and behavioral issues within the family and school contexts are also needed (Scharf & Williams, 2006).

This means that school psychologists, educators, and family members have an important role to play in the therapeutic intervention for children and adolescents with neuropsychiatric conditions. Children and adolescents with psychiatric conditions require support in managing and attenuating their symptoms in addition to addressing academic and social pressures. Parents can help ensure a proper treatment regimen by providing a family history of psychiatric illness and family members' responsiveness to certain psychotropic medications (Scharf & Williams, 2006). Parents can also help decide when medications should begin or change depending on events in the child's life, as well as monitor the child's or adolescent's adherence to the prescribed regimen (Scharf & Williams). Parents can also advocate for psychotherapy for their child, even as a first step before medication trials are initiated. Educators can assist parents by sending home daily or weekly reports of the child's behavior and/or symptoms, working closely with the child to ascertain if his or her symptoms are manageable, and working with the school multidisciplinary team to develop accommodations as necessary. Interventions using a multipronged approach, including psychosocial therapy, family supports, educational accommodation, and psychopharmacology (as needed), are likely to lead to more favorable outcomes for the individual than any single approach.