

The Road to Rehabilitation

Part 6 ■ Mapping the Way: Drug Therapy & Brain Injury

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Brain Injury Association of America

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Creating a better future through brain injury prevention, research, education and advocacy.

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Introduction

The basic unit of the nervous system is the neuron or nerve cell. Billions of these cells connect with one another to transmit information from one part of the brain to another. The messages are passed on by chemicals (neurotransmitters) released by one cell and absorbed by the next cell down stream.

With brain injury, the cell's ability to produce these neurotransmitters is reduced either by interference with production, release or absorption. These chemical changes alter the brain's ability to process information.

Medications prescribed after a brain injury improve the brain's natural ability to produce and utilize neurotransmitters. The medications act as a "cast" for the neuron to allow more normal activity during recovery. In situations where the neuron fails to recover its function, medications then are used as "splints" to allow the most "normal" neuron function possible.

Medication Selection is Based on Four Components

Target Symptoms

What problem is to be addressed by drug intervention? This could include problems such as: headache, insomnia, dizziness, depression and impulsivity. By defining the problem specifically, medication effect can be weighed against the likelihood of spontaneous improvement. Also, the underlying neurochemical problem can be addressed if the region of the involved area is known or if the problem has a known neurochemical deficiency.

Route of Administration

Can the medication be given orally, topically, by injection, by inhalation or by some other method? The speed of absorption largely is determined by the route which the medication is administered. Problems associated with toxic levels also can be accelerated, depending on how the medication is dispensed.

Onset of Action

How long does it take the medication to work? This factor depends upon the speed at which the medication crosses from the bloodstream into the neuron and the speed with which it alters the neurotransmitter activity.

Side Effect Profile

All medications have side effects and the risk/benefit ratio must be considered. This includes whether the side effects potentially are permanent, such as with tardive dyskinesia, or temporary, as with dry mouth.

Types of Medication Used After Brain Injury

Anticonvulsants

Anticonvulsants (i.e., carbamazepine, valproic acid, phenytoin, phenobarbital, tiagabine, lamotrigine, gabapentin, topiramate) act to prevent abnormal firing patterns of neurons. This can occur as a result of direct injury to the cell or due to chemical changes around the cell. These seizures either can be generalized or focal events. Focal seizures may involve sensory, motor or behavioral regions of the brain.

One way in which anticonvulsants (i.e., benzodiazepines, barbiturates, valproic acid) may prevent seizures is by increasing the activity of an inhibitory neurotransmitter, GABA. They also may decrease the firing rates by preventing the "snowball" effect of seizure production called kindling (i.e., carbamazepine).

Anticonvulsants can be used not only to prevent seizures, but also to: (1) decrease irritability, (2) improve frustration tolerance, (3) decrease headache and (4) stabilize mood swings. Balance problems also may respond to certain anticonvulsants.

Once these anticonvulsant medications are prescribed, follow-up blood testing may be required to ensure that the concentrations of medication in the blood falls within the therapeutic range. This is the level required to inhibit seizures in 95% of persons. These tests also may involve assessment of liver function and blood counts (CBC) to monitor potential toxicity of these agents.

Side effects commonly encountered with these agents include: fatigue (barbiturates, benzodiazepines), dizziness (phenytoin, carbamazepine) and gastrointestinal irritation (valproic acid). Abruptly stopping these medications without medical guidance can result in severe seizures and even death.

Antidepressants

Antidepressants were first developed in the 1940s, and many refinements have occurred in the years since. Types of antidepressants include monoamine oxidase inhibitors (MAOI), tricyclics (TCA), heterocyclics and specific serotonin re-uptake inhibitors (SSRI). Novel antidepressants also have been developed which have combination effects.

MAOIs (i.e., phenelzine, tranylcypromine) act by slowing the breakdown of neurotransmitters at the synapse (the junction where neural impulses are transmitted). The agents currently available require strict dietary control to prevent toxic reaction which will elevate blood pressure to lethal levels.

MAOIs tend to increase energy but may cause insomnia, even at low dosages. Prescription of these agents must be supervised closely to prevent accidental drug-drug interaction (i.e., avoiding meperidine, decongestants, diet pills).

TCAs (i.e., amitriptyline, imipramine, desipramine, nortriptyline, protriptyline, clomipramine) are related closely to antihistamines and possess many of the same characteristics. They act by decreasing the reabsorption of neurotransmitters into the releasing neuron (“re-uptake inhibition”).

No dietary restrictions are necessary with TCAs. They act to increase two neurotransmitters—serotonin and norepinephrine. Onset of action generally is two to four weeks after treatment is started. This allows the development of certain blood concentrations and then for the agent to cross into the neuron. Periodic assessment of blood level is useful to ensure an effective concentration.

Side effects with TCAs largely are caused by their antihistaminic and anticholinergic properties. They tend to be more sedating and commonly induce initial sleep improvement. They also tend to cause dry mouth, delayed urination, sexual dysfunction, constipation and lightheadedness. These side effects also can assist in alleviating some types of post-traumatic dizziness. Some cardiac changes may be evident, including increased heart rate and, rarely, skipped beats. TCAs also may lower the seizure threshold after brain injury. These medications can be used for: (1) explosive episodes, (2) emotional instability, (3) headache relief, (4) chronic pain management, (5) insomnia, (6) post-traumatic stress disorder and (7) typical depressive symptoms.

SSRIs (i.e., fluoxetine, fluvoxamine, sertraline, paroxetine, nefazadone, citalopram) are the newest agents in this class. SSRIs prevent the reabsorption of serotonin into the releasing neuron and increase its availability to the next neuron downstream. These powerful medications have a more rapid action onset. Usually, they have no cardiac side effects. Principle side effects relate to nausea, dizziness, fatigue and, occasionally, tremor. SSRIs also may cause sexual dysfunction. Interaction with anticonvulsants also can influence seizure threshold.

Novel antidepressants combine serotonin re-uptake inhibition with norepinephrine re-uptake inhibition (i.e., venlafaxine) or dopamine blockade (i.e., amoxapine). Side effects are similar to other agents. However, amoxapine may cause involuntary movements as can neuroleptics. Bupropion causes re-uptake inhibition of serotonin, norepinephrine and dopamine. It may be associated with over-stimulation or seizures.

Antianxiety Agents

Antianxiety agents (i.e., lorazepam, diazepam, alprazolam) exert their effect by increasing the inhibitory neurotransmitter, GABA. This then slows the firing rates of all neurons in the region. For thousands of years, alcohol has been used to do this as well. Currently used agents primarily are benzodiazepines, although barbiturates still are prescribed. The effect of these agents is to reduce the individual's awareness of environmental stress and disrupt memory of the events. Buspirone acts to decrease the impact of environmental events on aggression through interference with serotonin activity in the hippocampal/amygdala (memory processing) regions of the brain.

Side effects of GABA-potentiating agents include: (1) sedation, (2) short-term memory disruption, (3) muscle relaxation and (4) development of tolerance. They act to raise the seizure threshold and have some use as secondary anticonvulsants. These agents cannot be stopped without medical supervision as they can result in severe withdrawal delirium, including potentially lethal seizures. The use of ethanol with these agents greatly increases their sedating properties and can result in slowing or stopping breathing. Short-term use is appropriate if closely supervised by a physician.

Neuroleptics

Neuroleptics (i.e., chlorpromazine, haloperidol, thioridazine, risperidone, pimozide) act by blocking the transmission of dopamine-stimulated nerve impulses. They rarely are used for agitation and aggressive behavior, as studies have shown that they may slow the recovery rate after brain injury. Neuroleptics may be required in severe cases of delusional thinking or hallucinations. Other similar medications are used to decrease nausea and vomiting and enhance the effect of narcotic pain relievers.

Side effects include: (1) abnormal involuntary movements, (2) weight gain, (3) low blood pressure, (4) lowered seizure threshold and (5) decreased memory. Permanent movement disorders can be seen. Newer agents such as clozapine, olanzapine, ziprasidone and quetiapine are less likely to cause movement problems, although lowered production of blood cells can be observed with clozapine.

Anti-Parkinson Agents

Anti-Parkinson agents (i.e., levodopa, amantadine, bromocriptine, pergolide, pramipexole, ropinirole, benzotropine) act to increase dopamine activity or decrease cholinergic activity at the synapse. This may be beneficial in certain types of amotivational syndromes and initiation deficits. They are used to increase endurance—both cognitive and physical—and improve swallowing in certain individuals. They also can improve initiation and mood.

Side effects include: (1) agitation, (2) nausea, (3) blood pressure changes and (4) headache. High dosages also may induce hallucinations or paranoid delusions.

Psychostimulants

Psychostimulants (i.e., methylphenidate, dextroamphetamine, pemoline) are used to: (1) decrease daytime drowsiness, (2) increase attention and concentration and (3) increase mood temporarily. They act by increasing the release of already-produced norepinephrine and dopamine from storage areas of the neuron. Their onset of action is within hours, and their duration is usually less than 24 hours (with the exception of pemoline). Long-term use must be monitored closely by a physician because of the abuse potential and possible lowering of the seizure threshold. These agents also can trigger paranoid thoughts and insomnia. Modafinil is a new agent that is useful in combating fatigue associated with neurological dysfunction.

Anticholinergic Agents

Anticholinergic agents (i.e., meclizine, scopolamine) may be used to increase tolerance for certain types of dizziness, increase endurance and relieve insomnia at the beginning of the night. The ability of these agents to lower seizure threshold and to cause dry mouth, constipation and confusion at high doses requires close monitoring.

Antihypertensives

Antihypertensives are used for headache management, aggressive behavior and impulsivity. Beta blockers (i.e., propranolol, atenolol) were the first of this class to be used successfully. Side effects include lowered heart rate and blood pressure. The agents cannot be used in persons at risk for hypoglycemia, as they mask the physical complaints.

Certain medications (i.e., propranolol) also may increase depressive symptoms. Alpha blocking agents (i.e., clonidine) are used to decrease impulsivity and blood pressure. Calcium channel blockers (i.e., verapamil) have been used to treat migraine headaches after brain injury. Their primary side effects include light headedness and constipation.

Narcotic Antagonists

Narcotic antagonists (i.e., naltrexone) are a class of medications that block the brain's naturally produced opiates (endorphins) from attaching at receptor sites in the brain. These agents can be used to decrease self-injurious behavior, bulimic symptoms (bingeing and purging on food) and suicidality. These agents may decrease the craving for alcohol in those individuals with alcoholism. Side effects include potential liver irritation, confusion and headache.

Botox® (Botulinum Toxin Type A)

This unique agent that is injected into muscle, prevents the release of chemical transmitters that cause muscles to contract. While other chemicals (i.e., phenol, local anesthetics) have been used to reduce this increased contraction (spasticity), Botox® provides symptomatic relief of spasticity within three to seven days of injection. Repeated dosing may be necessary to achieve the desired reduction in tone. For more information on Botox® and spasticity after brain injury, see *Part 7: Spasticity Management*.

Dependence on Medication

Although not addictive in the typical sense of the word, these medicines all must be started and stopped under the supervision of a physician. If stopped abruptly, anticonvulsant and antianxiety medications can cause seizures and hallucinations. Stopping antidepressants too quickly can result in insomnia and agitation. Suddenly stopping antihypertensives can cause rebound elevation in blood pressure.

Side Effects

All medicines have a main therapeutic effect, as well as side effects. Your physician can work with you to find a medicine that works, while causing the fewest side effects. Occasionally, side effects must be tolerated if no other options exist.

Commonly Asked Questions

If I am not depressed, why do I need an antidepressant?

Antidepressants work by increasing the amount of either serotonin or norepinephrine at the neuronal connections called synapses. In addition to depression, this effect may be useful in: (1) vascular headache management, (2) chronic pain syndromes, (3) sleep disorders and (4) balance problems. Some degree of depressed mood is expected after a brain injury because of the reaction to the changes experienced. When these mood changes are severe or include early morning awakening, appetite change, weight loss or gain and other neurovegetative symptoms, antidepressants may be indicated.

If I am not having seizures, why do I need an anticonvulsant?

Anticonvulsants act to decrease the irritability of the neuron. In the most extreme situation, a seizure occurs. This irritability also can cause agitation, aggressiveness and headache. The use of an anticonvulsant may help.

When can I stop my medication?

Before stopping your medications, you always should inform your physician. If you develop a serious side effect, contact your doctor or go to the nearest emergency room. Be sure to bring all your medications with you, so the physician will know exactly what you are taking.

Can I take over-the-counter medicines, vitamin supplements or health foods?

You need to check with your physician first. While some medications will not be affected, others may either increase or decrease their effectiveness when combined with these substances.

Can I drink a beer, a glass of wine or a mixed drink with my medicines?

Mixing alcohol with your medicines is not a good idea. Although some physicians allow moderate use of alcohol, if no previous history of substance abuse exists, any amount of alcohol may alter the effectiveness of these medications.

Can I use other recreational drugs?

No. If you do experiment in this manner, you may counteract the positive effect of your medications. Discuss your thoughts with your physician to find another method to deal with stress.

Where can I go for more information?

Contact BIA at (800) 444-6443 for names of physicians in your area who specialize in medication management.

About the Author...

Gregory O'Shanick, MD, has worked since 1981 in all aspects of neuropsychiatry and neurorehabilitation. After 10 years in academic medicine and research, he founded the Center for Neurorehabilitation Services in Midlothian, VA, where he is Medical Director. In 1996, he was asked to be the first National Medical Director for BIA. He enjoys an international reputation and has authored over 75 scientific publications in prevention, evaluation and intervention in acquired brain injury (ABI).

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For additional information about dealing with post-traumatic headaches and brain injury, contact BIA's Family Helpline at (800) 444-6443 or familyhelpline@biausa.org. Or visit BIA's award-winning web site at: www.biausa.org.

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Road to Rehabilitation Series

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7. Traveling Toward Relief: Dealing with Spasticity and Brain Injury
8. Journey Toward Understanding: Concussion and Mild Brain Injury

For the individual with brain injury and his/her circle of support (i.e., family members, significant others, friends and co-workers) brain injury is a complex and often tumultuous journey. Although there are broad issues affecting ALL individuals with brain injury, both the road to rehabilitation and the outcome experienced by each individual are unique. In this series of brochures, BIA seeks to educate individuals and organizations about rehabilitation after brain injury. Some individuals with brain injury may face challenges in all of these areas, while others may experience problems with just a few of them. Regardless, the information in these brochures is crucial to provide those affected by brain injury, as well as the individuals and organizations treating them, with a basic understanding of the complex challenges following brain injury. For additional information about any of the topics covered in The Road to Rehabilitation Series, contact BIA's toll-free Family Helpline at (800) 444-6443 or visit their web site at www.biausa.org.