BONUS CHAPTER

Medications and Your Anxious Brain

After reading our book *Rewire Your Anxious Brain*, you have an understanding of the various pathways in the cortex and amygdala that underlie or influence the experience of anxiety. In this bonus chapter, we'll examine how medications and other drugs affect these processes. We hope you now understand that learning to resist fear is an active process, not a passive one that can be accomplished solely by taking medications to erase anxiety; the brain doesn't work that way. Medications can help you cope, especially in the short term. But no medication has been designed that will rewire a circuit or form new connections in the absence of *experience*. You need to seek experiences and deliberately modify your thoughts to change the circuitry.

The brain is a living, changing organ that has the potential to modify and rewire itself with each new event you experience. The substances you introduce into your brain can promote changes its structure and functioning, but can't accomplish rewiring the way exposure experiences can. Studies have shown how essential such experiences are in the process of changing brain circuitry in the amygdala (McLean et al. 2015). Research on the cortex has shown that the way people choose to think, imagine, and interpret their experiences changes neural circuitry throughout the life span.

However, anxiety often limits a person's willingness to change. Fears can shrink the world down to narrow confines. We avoid places, don't challenge ourselves, or restrict our interpersonal activities. As a result, we don't provide the brain with opportunities to learn how to resist the old patterns of anxiety-producing thoughts. Avoidance of change preserves the state the brain is in, keeping it stuck in old patterns. In this way, life becomes a vicious, fear-perpetuating circle of anxiety-based behavior.

The Role of Medications

Medication may be necessary to help some people interrupt the vicious circle of anxiety. Certain anxiety disorders, such as phobias, usually don't require medication to be overcome because they appear to be less limiting and can be treated successfully with exposure. Other anxiety disorders may require sufferers to take medication temporarily; still others may require sufferers to take it for the rest of their lives, depending on the pervasiveness of the disorder. In this bonus chapter, our goal is to help you understand how antianxiety medications affect the process of training the brain to resist the detrimental effects of the defense response.

Medication can be helpful in reducing anxiety, but always remember that, by itself, medication won't provide you with the learning experiences like exposure that stimulates your brain to build new circuitry and weaken old connections (Hauner et al., 2012; Helpman et al., 2014). In fact, some medications interfere with the brain's ability to rewire itself and learn to resist

anxiety. For this reason, we'll address not only the short-term effects of common anxiety medications in terms of reducing anxiety, but also the way they affect the rewiring of anxiety-related circuitry in the cortex and amygdala pathways. Rewiring this circuitry is what accomplishes lasting change.

Weigh the Pros and Cons with Your Doctor

A variety of medications have been found helpful in treating anxiety disorders, but none of them are seen as ideal for every person. While selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are considered the first-line treatment for many anxiety disorders (Bandelow et al. 2012;), each individual needs to work with his or her physician to identify the best approach. This chapter is not intended to replace appropriate medical treatment and cannot be substituted for the advice of physicians or therapists who are familiar with your situation. Rather, this chapter will outline relevant information that you should consider when you discuss medications with health care practitioners and make decisions about whether to take them.

An important issue you should discuss with your practitioner is whether you're using medication for long-term change or short-term relief. Some medications aren't intended to be used for more than several weeks. For many antianxiety medications, when use is discontinued, problems with anxiety often return. In fact, in some cases—such as with the use of benzodiazepines—anxiety and insomnia may actually become *worse* after the medication is discontinued (Manconi et al. 2017; Vicens et al. 2011). Other medications that are effective in suppressing anxiety often must be taken for a long time to maintain their results (Koen and Stein 2011). So it's important to consider how long a medication can be safely used and what will happen when you stop taking the medication.

Another important consideration is the effect of medication on therapy. Some medications have been shown to increase or decrease the effectiveness of various therapeutic approaches. The right combination of medication and treatment can also vary depending on what phase of treatment you're in. Be sure to discuss all of this with your doctor and therapist to ensure your treatment plan will help you achieve the most beneficial outcome.

Exercise: Review Your Medications

In the table below or on a blank piece of paper, list the medications you've taken to treat your anxiety and identify what category each falls into—benzodiazepine, SSRI, SNRI, beta-blocker, and so on. (You may need to consult http://www.rxlist.com or http://www.medlineplus.gov to determine the category. The individual categories will also be identified later in this chapter.) Then describe the effects of each medication—both positive and negative effects, including side effects.

Medication	Category	Positive Effects	Negative Effects

How Antianxiety Medications Affect the Brain

Treatment with medication is most effective when its effects are understood and the medication is used strategically. After reading this chapter, you'll be better informed about how medications can enhance, complement, or interfere with your ability to rewire your brain to reduce the effects of anxiety. While we'll do our best to explain the effects of specific medications, the truth is that we still don't know exactly how some of the medications discussed exert the effects they have on the brain. Consulting the *Physician's Desk Reference* (PDR Staff 2015) will readily validate this surprising state of affairs. If you check the information on mechanism of action for many antianxiety medications, you'll often find the statement "Their exact mechanism of action is unknown."

Research is underway to identify exactly how certain medications affect brain processes, but a surprising number of medications are prescribed for their effects on anxiety despite the fact that no one knows exactly how they work. (By the way, this lack of knowledge not only happens with antianxiety medications; the process by which aspirin, or salicylic acid, reduces pains was only identified in the 1970s, despite it having been used for centuries.)

When considering how a medication works, keep in mind that a drug that's very good at reducing anxiety won't necessarily change the processes in the brain that create anxiety; just because a medication relieves a problem doesn't mean it targets the underlying cause.. Again, aspirin provides a helpful analogy (Coplan and Lydiard 1998). Imagine that you cracked a tooth

on hard candy and subsequently developed an abscess in the tooth. As a result, you experienced a toothache. If you took aspirin and the toothache disappeared, would it be correct to assume that your difficulties were due to a shortage of aspirin in your system? Would it make sense to say that your problems were due to an "aspirin imbalance" and that regular use of aspirin would correct the problem? Obviously not!

The point is, we must be cautious about assigning reasons for a medication's effectiveness. Fortunately, both laboratory research and new brain-imaging studies are helping shed light on the areas in the brain that are affected by specific medications. These advances offer helpful guidance on how to use medications for anxiety, which we'll share below.

That said, studies examining the long-term effects of medications on the brain are few and far between. Most drugs used for the treatment of anxiety disorders have been approved on the basis of their short-term effects; little information exists regarding the long-term effects of many medications, since such research is costly. And most studies of medications consider periods of one year or less sufficient for a "long-term" study (for example, Mavissakalian et al. 2002; Allgulander et al 2002). Therefore, even though people often take certain medications for decades, there isn't much information about how this long-term use affects the brain.

Side Effects

Side effects are unintended adverse consequences associated with taking medication. In the case of antianxiety medications, side effects can range from stomach upset to confusion and from muscle weakness to sexual dysfunction. There are a few reasons for this. First, keep in mind that brain functions rely on neurotransmitters, chemicals that allow neurons to communicate with each other. The brain—and the rest of the body—uses a limited number of neurotransmitters in multiple neurological processes. Just as you can use baking soda for a variety of purposes (for leavening, as a cleaning agent or toothpaste, to deodorize your refrigerator, and so on), the human body uses most neurotransmitters in a variety of different systems.

Therefore, medications designed to influence a neurotransmitter's activity in one set of brain circuits may also have the "side effect" of influencing completely unrelated processes. Consider serotonin, a neurotransmitter often thought to be involved in various areas of the brain that create anxiety. However, medications used to increase serotonin levels in the brain may also affect intestinal processes because serotonin plays a key role in coordinating motility in the intestines. This results in side effects that can include constipation or diarrhea.

Because it's very difficult to impact levels of a neurotransmitter in a specific location without influencing other parts of the nervous system, side effects—like interference with sleep patterns or sex drive—are likely with some medications people take for anxiety. Furthermore, levels of one neurotransmitter in the brain may shift in response to changes in levels of other neurotransmitters. Therefore, it's difficult to make one isolated change in the brain without affecting other systems. When you combine medications, the effects just described become even more complicated. Finally, because no two brains or bodies are exactly alike, medications frequently have different effects on different people. So a medication that's helpful for one person may have only negative effects for another person.

For all of these reasons, no one can predict the response a specific individual will have to a specific medication. Under a doctor's supervision, a person may have to try a few different medications before finding the one that works best. This is normal practice.

New side effects can also develop after long-term use of a medication. The brain is a responsive and adaptive system, and it adjusts to changes in its chemistry in complex and sometimes unexpected ways. The continued presence of certain medications can lead the brain to change its structure or reduce its production of specific chemicals. And long-term impacts on the brain other than those intended for treatment can occur. However, we know very little about these effects because they're rarely studied. Pharmaceutical companies that design and evaluate medications tend to focus primarily on their short-term benefits and safety, and as mentioned, clinical trials of the effects of a medication rarely last more than one year.

Unintended short-term effects and unexpected long-term effects are both probable consequences of using medications to control anxiety. Both in this chapter and more widely, you'll see specific side effects mentioned for the medications described below. But because each individual is unique, and because medication effects are known to vary depending on ethnicity, gender, and age, the side effects a specific person might experience can't be predicted with certainty. Be sure to consult with your doctor so that you know the side effects of any medications you plan to take as part of your treatment.

Categories of Antianxiety Medications

Let's take a closer look at specific kinds of medications. The most commonly prescribed antianxiety medications fall into three categories: benzodiazepines, SSRIs and SNRIs, and beta-blockers. Each kind of medication attempts to reduce anxiety in a different way and has different influences on the process of rewiring the brain. You will be more likely to benefit from a medication if you know what to expect from it and use it in a way that promotes the changes you hope to produce.

Benzodiazepines

Benzodiazepines, medications such as Valium (diazepam), Xanax (alprazolam), Ativan (lorazepam), and Klonopin (clonazepam), have calming effects and, unlike many other medications, provide immediate relief from anxiety. They are often called anxiolytics (from *anxi*, meaning "torment," and *lytic*, meaning "to loosen") because they are so effective at reducing anxiety. Benzodiazepines improve people's ability to sleep and are often prescribed for insomnia. They may cause immediate side effects such as sedation, nausea, or muscle weakness; and combining benzodiazepines with alcohol can be fatal. Long-term side effects of benzodiazepines may include impairment in a variety of cognitive skills, including verbal learning and memory (Westra et al. 2004). Furthermore, impairment of memory and other skills may persist even after individuals stop taking benzodiazepines (Barker et al. 2005).

Daily use of benzodiazepines leads to *physiological dependence*, meaning dosages may need to be increased to sustain their effectiveness, and symptoms of withdrawal are likely if daily use is discontinued. Occasional use will not cause these issues. Symptoms of withdrawal may include insomnia, agitation, anxiety, panic attacks, depression, poor memory, headache, and seizures (Edinoff et al., 2021b). Some symptoms resemble anxiety, which can lead people experiencing withdrawal to believe their anxiety disorder is worsening. This is known as *rebound anxiety*. One can successfully discontinue daily use of benzodiazepines through a gradual, lengthy tapering of the medication, but this should be approached cautiously and under the care of a physician. Negative effects, including seizures, are possible if discontinuation happens too abruptly.

Note: Because of the potential for dependence, benzodiazepines shouldn't be used on a long-term basis, especially since evidence indicates that daily use for longer than three to four weeks can result in physiological dependence (Brett and Murnion 2015; Julien 2013). The number of people seeking treatment for benzodiazepine withdrawal problems is increasing (Edinoff et al., 2021b). Frequently, a person will assume anxiety is getting worse, having no idea the problem is physiological dependence.. Benzodiazepine dependence does not typically result from people taking more medication than prescribed; it develops simply as a result of prescribed daily use (Cloos 2010). If you rely on benzodiazepines daily, we strongly encourage you to seek a physician's help in determining whether your use of the medication is dangerous. Benzodiazepine dependence is a frequently neglected problem that can worsen anxiety rather than improve it (Julien 2013)..

How Benzodiazepines Affect Anxiety

Although the precise mechanism by which many benzodiazepines affect anxiety is unknown (PDR Staff 2015), these drugs are thought to calm the defense response by increasing the effects of a neurotransmitter called gamma-aminobutyric acid (GABA). GABA inhibits the activity of neural circuits in the amygdala (and many other parts of the brain and body). In other words, benzodiazepines provide a "GABA boost," slowing neuron activity in the amygdala and thereby reducing anxiety. As a result, benzodiazepines reduce fear-related responses, such as defensive behaviors (like escaping or freezing), as well as sympathetic nervous system responses (like sweating or increased heart rate). The common wisdom is simply that benzodiazepines tone down anxious responding by inhibiting the amygdala.

GABA is a key neurotransmitter throughout the brain; in fact, over one-third of the connections in the brain are GABA based. So the influence of benzodiazepines isn't restricted to fear circuitry. Benzodiazepines have effects on general GABA-related inhibition in other neural networks. Side effects such as sedation, muscle weakness, balance problems, and impaired memory and concentration result from the widespread inhibiting influence of GABA in many areas (Edinoff et al. 2021b; Julien 2013).

How Benzodiazepines Affect the Rewiring Process

Because benzodiazepines have a tranquilizing effect on the amygdala, they keep fear and anxiety in check. Unfortunately, this restraint on activation also impairs the learning process (Westra et al.

2004). Remember, the process of changing anxiety responses is based on creating new connections (Hauner et al., 2012; Helpman et al., 2014). You must *activate* neurons to *generate* new learning. New learning (rewiring) is less likely to occur in a brain medicated with benzodiazepines. Perhaps this is why multiple studies have found that the people who benefit most from psychotherapy and exposure are those who aren't taking benzodiazepines (Addis et al. 2006; Ahmed, Westra, and Stewart, 2008). Because neurons must fire if they are to rewire, benzodiazepines have the general effect of slowing the process of rewiring. The amygdala can't learn well while it's sedated.

In summary, benzodiazepines act to calm the amygdala and cortex, but they also preserve the system as it's currently wired. It seems that benzodiazepines restrict the brain's ability to create new connections that would allow for alternative responses, making the rewiring of established anxiety responses less likely. In a sedated amygdala, exposure exercises in particular might be unable to create new learning. If your goal is simply to reduce anxiety at a specific time or for a short period (several weeks at the most), short-term benzodiazepine use can be helpful. However, when attempting to retrain your brain to resist anxiety, in therapy or exposure, benzodiazepines are likely to interfere with the rewiring process (Julien 2013). Couple this drawback with the negative side effects of benzodiazepines, some of which may be long lasting, and you see why benzodiazepine use is not the first line of treatment for anxiety disorders (Durand et al., 2024.

SSRIs and SNRIs

Selective serotonin reuptake inhibitors (SSRIs) include medications such as Zoloft (sertraline), Prozac (fluoxetine), Celexa (citalopram), Lexapro (escitalopram), and Paxil (paroxetine). *Serotonin-norepinephrine reuptake inhibitors* (SNRIs) include medications such as Effexor (venlafaxine), Pristiq (desvenlafaxine), and Cymbalta (duloxetine). Both of these categories of medications are associated with the treatment of depression and are often called antidepressants, but they frequently have positive effects in people suffering from anxiety, for a couple of reasons. First, the fact that SSRIs and SNRIs reduce depression is beneficial for many people with anxiety because they are often also dealing with depression. Second, SSRIs and SNRIs have been shown to reduce anxiety when prescribed for a variety of anxiety disorders, and are the first line of treatment for anxiety disorders (Edinoff et al., 2021a). Unlike benzodiazepines, however, these medications don't provide immediate relief; they must often be taken for one to two weeks before people notice any beneficial effects (Preston and Johnson 2014). In fact, these medications may have the effect of increasing anxiety at first, and for that reason, some people start using them gradually, building up to the recommended dose over time (Preston and Johnson 2014).

Side effects associated with SSRI use include dry mouth, nausea, nervousness, insomnia, drowsiness, weight gain or loss, dizziness, headache, and sexual dysfunction (Edinoff et al., 2021a). Side effects associated with SNRIs are similar, but are less likely to include weight gain and more likely to include loss of appetite, sweating, agitation, and increased blood pressure (Chang et al., 2022). While these medications aren't addictive, discontinuing them may cause symptoms of withdrawal, including dizziness, headache, gastrointestinal difficulties, sensory disturbances (tingling, for example), agitation, anxiety, and sweating. The occurrence of these withdrawal symptoms has been named *antidepressant discontinuation syndrome*. To prevent this condition, it's

important to discontinue these medications gradually and cautiously, and under the care of a physician.

How SSRIs and SNRIs Affect Anxiety

These medications are called *reuptake inhibitors* because they block the process of reuptake—or reabsorption—of neurotransmitters by neurons. As discussed in chapter 1 of *Rewire Your Anxious Brain*, neurons communicate with each other by releasing neurotransmitters. After a neuron releases a neurotransmitter, it doesn't simply allow the neurotransmitter to remain in the synaptic space; instead, it reabsorbs the neurotransmitter for future use. This reuptake process is blocked by these medications, and the neurotransmitter is allowed to remain active in the space longer. This increases the activity of the receiving neurons, since the neurotransmitter is what carries the message to the next neuron. Therefore, medications that block reuptake increase the activity of neurons in the pathways they target. While SSRIs target neurons that use serotonin, SNRIs target neurons that use either serotonin or norepinephrine; therefore, SNRIs have an effect on a greater number of neurons. While these medications are known to exert their effects by increasing the activity of specific neurons in the brain, the way in which this additional activity affects anxiety is complex and not completely understood.

Let's start by looking at the SSRIs, which result in increased serotonin in the brain. Neural systems affected by increased serotonin regulate sleep, appetite, and digestion. Not surprisingly, the first drugs designed to affect serotonin levels often caused side effects of drowsiness, weight gain, and nausea. Over time, the medications have been refined to better target only specific serotonin receptors (and thus are called *selective* serotonin reuptake inhibitors). As a result, the number of side effects has generally been reduced. Generations of SSRIs have developed, with each newly named SSRI (for example, first Prozac, then Celexa, then Lexapro) tending to be more selective in terms of the types of serotonin receptors it affects.

As for what areas in the brain SSRIs affect, recent animal and human studies suggest that the amygdala and other brain areas, such as the hippocampus and parts of the frontal lobe, are impacted (Lukow et al. 2024; Song et al. 2019). In addition, research indicates that the anterior cingulate cortex is affected (Spindelegger et al. 2009). However, it will probably take years to sort out exactly what is happening in the brain. Only as technology advances and allows us to examine the effects on specific neural pathways will we truly understand all the areas in the brain that are being affected.

In the meanwhile, here's a summary of what we do know: At first it was thought that simply increasing levels of serotonin was responsible for reducing symptoms associated with anxiety and depression. This was consistent with the popular idea that depression resulted from a chemical imbalance of serotonin. But if the increased level of serotonin itself were responsible for the change in symptoms, the effects of increased serotonin would register immediately, as soon as people take the medication. Instead, it usually takes a week or more for a positive change in symptoms to occur (Bandelow et al., 2012). (And as mentioned, some people even experience a worsening of anxiety symptoms at first.) It therefore became obvious that the increase in serotonin levels couldn't be responsible for the delayed improvement, so researchers began investigating

other changes in neurons that took place in seven to fourteen days, when the medications began to ease the symptoms of anxiety.

What researchers found is that daily use of SSRIs for more than a week or two eventually results in changes in the *structure* of neurons. This is neuroplasticity in action. As the neurons adapt to getting more serotonin, they make adjustments in the number of receptors, grow new dendrites, or even promote the development of new connections or circuits (Eisch et al. 2008). Changes in brain-derived neurotrophic factor (BDNF) a chemical that plays a key role in neuron development, growth, and function, were also associated with several weeks of use of SSRIs (Lee et al., 2020). In other words, new, higher levels of serotonin may somehow stimulate neurons to remodel themselves and their circuits in a variety of ways. This process is currently only partially understood; for now, the most accurate way to characterize the change in these neurons is to call it increased flexibility, indicating that the neurons become more capable of modification. Thus, SSRIs are thought to increase the brain's ability to restructure parts of itself, making it more amenable to new learning.

Next, let's look at which neural systems are affected by SNRIs, which increase levels of both serotonin and norepinephrine. Once again, a variety of neural systems use norepinephrine as a neurotransmitter, and both the amygdala and the hippocampus are affected. Research has also shown that norepinephrine has influences on the thalamus and prefrontal areas of the cortex (Frodl et al. 2011). In addition, it regulates systems in the body involved in heart rate, breathing, and blood flow to the muscles. As with SSRIs, it is the longer-term effects of SNRIs that are helpful with anxiety. In fact, like SSRIs, SNRIs frequently increase anxiety at first, so they too should often be started gradually. After a week or so, the higher levels of serotonin and norepinephrine may stimulate neurons to remodel themselves and their circuits in a variety of ways that promote increased flexibility. So it seems that both SSRIs and SNRIs may make the circuitry in the brain more capable of being modified.

Interestingly, therapists sometimes heard descriptions of this type of experience from clients long before the technology was available to detect specific changes in the neurons. Therapists reported that their clients said using these medications seemed to give them more control over what they thought—that they didn't feel so stuck in certain thought patterns. Perhaps this is how it feels to experience increased neural flexibility. It wasn't that the medication resulted in new thoughts, but that people felt an increased flexibility in thinking that gave them the ability to create new thought patterns. For example, they were better able to change the focus of their attention or stop dwelling on certain situations or thoughts. This brings us to the next topic…

How SSRIs and SNRIs Affect Rewiring in the Fear System

Research on the effects of SSRIs and SNRIs hasn't yielded definitive answers about how these medications affect the cortex and amygdala. Because research indicates that SSRIs promote growth and change in neurons (Molendijk et al. 2011), it's possible that the process of rewiring the amygdala and cortex is enhanced by SSRIs. Therefore, they may make it more likely that a circuit in the brain can be modified by experience. However, at this time it isn't possible to predict the specific location or nature of the rewiring.

But clearly, promoting the growth of neurons is of great significance. A gardening analogy might prove useful at this point. Imagine that taking these medications is similar to using fertilizer in your garden to promote new growth. You see more roots, branches, and buds. Of course, you need to be careful what you fertilize; the weeds will respond just as quickly as the roses if you aren't careful! Taking care to examine which neural patterns you're strengthening would seem to be significant in making effective use of SSRI or SNRI treatment. This means it's important to consider what you're teaching your brain when you take these drugs. Research indicates that they are most helpful in changing people's thought processes when combined with therapy focused on modifying specific self-defeating thoughts (Wilkinson and Goodyer 2008).

At this time, it seems reasonable to hypothesize that SSRIs and SNRIs have the potential to assist efforts to rewire the neural circuits underlying fear and anxiety responses in both the amygdala and the cortex. This hypothesis is supported by the fact that combining these medications with psychotherapy often produces quicker, more positive outcomes than when psychotherapy is used alone (Van Apeldoorn et al. 2013). Perhaps in the near future, brain imaging research will clarify the exact effects of these medications on neural circuitry.

Beta-Blockers

Beta-blockers, which include medications such as Inderal (propranolol), Tenormin (atenolol), and Toprol (metoprolol), don't reduce anxiety itself, but instead reduce symptoms associated with anxiety, such as trembling or increased heart rate. Beta-blockers control these symptoms by blocking certain receptors for adrenaline (beta-adrenergic receptors), keeping adrenaline from having its usual effects (Archer et al. 2025). Side effects such as reduced blood pressure, dizziness, tiredness, and even insomnia can occur with the use of beta-blockers (Archer et al. 2025). Side effects associated with long-term use haven't been well studied, but some investigations suggest that chronic use can result in impaired memory (Nielson 1994).

Beta-blockers aren't addictive, and long-term effects aren't expected when they're taken infrequently (for example, when a beta-blocker is prescribed for a violinist to take before an anxiety-provoking concert performance). However, daily use of these drugs does lead to physiological dependence, so symptoms of withdrawal, such as sweating or increased blood pressure or heart rate, are likely when the medication is discontinued. Because so many of the symptoms of discontinuing beta-blockers resemble anxiety, this can lead people to believe that their anxiety disorder is worsening. For these reasons, daily use of beta-blockers shouldn't be halted abruptly. As is often the case, it is best to do so gradually and under the care of a physician.

How Beta-Blockers Affect Anxiety

As discussed in chapter 5 of the book, the fight, flight, or freeze response occurs when the central nucleus of the amygdala activates a variety of body systems to prepare the body to react to a threatening situation. The amygdala causes the hormone adrenaline to be released into the bloodstream from the adrenal glands. Importantly, adrenaline is not just a hormone; it's also a neurotransmitter that carries the message to react to stress throughout the entire body. Beta-

blockers prevent or reduce specific symptoms associated with the fight, flight, or freeze response by occupying the receptors for adrenaline, thus blocking adrenaline's effects (Archer et al. 2025). As you may recall from chapter 5, adrenaline is responsible for increased heart rate, elevated blood sugar, and increased blood flow in the legs and arms, all of which prepare the body to respond to a threat by running or fighting. Therefore, beta-blockers prevent adrenaline from shifting the body into this state of heightened activation.

When you take beta-blockers, you aren't affecting the amygdala directly; it still reacts to the situations you experience, and it still sends signals to produce adrenaline. But symptoms such as increased heart rate, trembling, and sweating will be reduced because adrenaline can't effectively trigger these reactions. So rather than preventing anxiety per se, beta-blockers reduce the body's responses to perceived threats.

How does this affect the cortex? Anxious thoughts and worries in the cortex aren't directly reduced by beta-blockers. You can still worry, but your physical symptoms may be diminished. People with *anxiety sensitivity*, meaning those who are very aware of and anxious about physical sensations, may find this reduction in stress symptoms to be a relief.

How Beta-blockers Affect Rewiring in the Fear System

Beta-blockers don't have a direct impact on the process of rewiring neural circuitry in the brain. Fears and anxieties already wired into the amygdala aren't affected, although the body's responding to them is minimized. There is some indication, though, that in certain cases, beta-blockers might be helpful in preventing fear associations from developing into anxiety-provoking memories.

Fear-related memories are especially problematic in post-traumatic stress disorder (PTSD), in which people keep reliving or vividly remembering a catastrophic event. Some evidence indicates that the reason certain memories are so strong and frequently recalled is that, during the traumatic experience, adrenaline's effect on the brain intensifies some memories. They become "super memories," if you will. Studies are looking into ways beta-blockers might be used to prevent this from occurring. For example, if adrenaline operates to enhance memories of events that evoke powerful emotions, then giving beta-blockers to people who have just experienced a traumatic event, like a battle or a sexual assault, might prevent their brain from forming the type of enduring memories that often haunt survivors of these events.

Studies have shown mixed results regarding whether Inderal (propranolol) administered after exposure to trauma reduces the symptoms of PTSD (Stein et al. 2007). These results are preliminary, however, and seem to depend on the amount of beta-blocker administered and the timing of the medication. Still, this research is an example of how we can apply knowledge about how fear is created in the brain.

A New Use for an Old Medication

While scientists are trying to develop new medications for the treatment of anxiety disorders, an old medication, originally developed for the treatment of tuberculosis, has shown some promise in assisting in the learning process during exposure. This medication, D-cycloserine, has long been approved by the Food and Drug Administration; it is also available in generic form, and is therefore very reasonably priced.

The use of D-cycloserine is not focused on reducing symptoms of anxiety. In fact, it doesn't appear to affect the experience of anxiety at all. Instead, it is being studied because of its effects on neurons involved in learning in the amygdala (Davis et al. 2005). Researchers first found that D-cycloserine could improve learning in rats. Interestingly, experiments also found that D-cycloserine helps the amygdala learn during exposure (Walker et al. 2002).

Researchers discovered that people who took D-cycloserine during exposure exercises exhibited better learning (greater reduction in fear or quicker improvement) than those who didn't take the drug. Some studies have shown that the drug facilitates exposure therapy in a variety of anxiety disorders, including social anxiety disorder (Hofmann et al. 2013), PTSD (Rothbaum et al. 2014), and obsessive-compulsive disorder (Kushner et al. 2007). In short, researchers have found a drug that seems to facilitate the process of teaching the amygdala to rewire circuits! For example, after two exposure sessions while taking D-cycloserine, people who had severe fear of heights experienced a great reduction in their fear, a change that typically takes seven or eight sessions without D-cycloserine (Davis 2010). Medications such as this, which work to facilitate learning during the process of exposure, offer some hope for people who suffer from anxiety. At this point, D-cycloserine hasn't been widely used in the treatment of anxiety, and researchers are continuing to experiment to determine appropriate dosages and how best to use it (Schade and Paulus, 2016) but past research indicates that it has few side effects (Davis et al. 2005).

Summary

In this chapter, we've provided information on the medications most commonly used to treat anxiety. Although it currently isn't possible to identify the exact effects each medication has on the brain, it appears that SSRIs and SNRIs show promise in terms of their ability to facilitate neural flexibility, and that they may be helpful in the process of changing the circuitry underlying anxiety in both the cortex and the amygdala. In contrast, benzodiazepines seem to be more likely to interfere with the process of changing neural circuitry, especially in the amygdala, since they reduce the amygdala activation required to generate new connections. Beta-blockers seem to neither facilitate nor impair the process of rewiring; instead, they simply prevent people from experiencing many of the physical aspects of anxiety.

With the information in this bonus chapter, you can discuss medications in a more informed way with your physician, therapist, or psychiatrist. Considering the effectiveness of short-term and long-term use of medications and their side effects, as well as the effectiveness of the medication on both anxiety reduction and lasting change in the brain, can be of benefit in communicating about your treatment plan. Unfortunately, because every person is different and

needs to examine what effects they experience from a given medication, multiple medications may need to be tried before finding the right one(s). As more of the processes underlying anxiety are illuminated by researchers, drug manufacturers will hopefully learn to directly target these processes. Although we do not have evidence that medications are specifically addressing or correcting specific dysfunctions that cause the different anxiety disorders (Muse et al. 2013), we do know ways to promote general changes in the anxious brain that help give anxiety sufferers more control of the process.

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