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 change its structure and functioning, but so can each encounter you have with your fears. Studies have shown how essential such experiences are in the process of shaping brain circuitry in the amygdala. 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 ability 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 psychotherapy. 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 anxiety response.

Medication can be helpful in reducing anxiety, but always remember that, by itself, medication won't provide you with the learning experiences that will allow your brain to weaken old patterns of responding and build new circuitry. In fact, some medications actually 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; Hoffman and Mathew 2008; Koen and Stein 2011), 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. Other medications that are effective in suppressing anxiety often must be taken for a long time to maintain their results (Koen and Stein 2011). And for many antianxiety medications, when use is discontinued, problems with anxiety often return. In fact, in some cases—such as with the long-term use of benzodiazepines—anxiety and other problems may actually become *worse* after the medication is discontinued (Vicens et al. 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

Obviously, 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, it's important to understand 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 2012) 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 why or how they work. (By the way, don't assume that this state of affairs is specific to antianxiety medications; the process by which aspirin, or salicylic acid, achieves its effects 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 cause of the underlying problem. 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 and a low-grade fever. If you took aspirin and both the toothache and fever 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, Perel, and Guo 2002; Allgulander, Hirschfeld, and Nutt 2002). Therefore, despite the fact that people often continue to take certain medications for decades, there isn't much information about how their 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 any 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.

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 about the side effects of any medications you take or 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).

Prolonged use of benzodiazepines leads to *physiological dependence*, meaning increased dosages may be needed to sustain desired effects, and symptoms of withdrawal are likely if the medication is discontinued. Symptoms of withdrawal may include insomnia, agitation, anxiety, headache, and loss of appetite. Some symptoms of withdrawal resemble anxiety, which can lead people who are going through withdrawal to believe that their anxiety disorder is worsening. This is known as *rebound anxiety*. It is possible to successfully discontinue benzodiazepines through a slow tapering of the medication, but this should be approached cautiously and under the care of a physician. Negative effects, including seizures, are possible if the medication is discontinued too quickly.

Note: Because of the potential for dependence, benzodiazepines shouldn't be used on a long-term basis (Hoffman and Mathew 2008), especially since evidence indicates that daily use for longer than

four to six weeks can result in physiological dependence (Rivas-Vazquez 2003). People who use benzodiazepines occasionally are unlikely to experience dependence, but those using them daily risk dependence, which can lead to a variety of withdrawal symptoms, including insomnia, physical complaints, and heightened anxiety (O'Brien 2005). Frequently, a person will assume anxiety is getting worse, having no idea that the problem is physiological dependence on benzodiazepines. Benzodiazepine dependence does not typically result from people taking more medication than prescribed; dependence is more likely to develop 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 (Petursson 1994).

How Benzodiazepines Affect Anxiety

Although the precise mechanism by which many benzodiazepines affect anxiety is unknown (PDR Staff 2012), it is thought that these drugs calm the fear response by increasing the effects of a neurotransmitter called gamma-aminobutyric acid (GABA). GABA inhibits the activity of neural circuits in the amygdala (and 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 the brain's fear circuitry. Benzodiazepines also have effects on general GABA transmission and increase many inhibitory processes in other neural networks. Side effects such as sedation, muscle weakness, and impaired concentration result from the inhibiting influence of GABA in these other networks (Koen and Stein 2011).

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. 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 therapy 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. This may also explain why studies have found that taking benzodiazepines decreases the effectiveness of exposure-based treatment (Addis et al. 2006).

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. This suggests that 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, especially through exposure, benzodiazepines are likely to interfere with the rewiring process. 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 recommended as a first line of treatment for anxiety disorders (Koen and Stein 2011).

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 variety of anxiety disorders (Koen and Stein 2011). 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. 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.

Side effects associated with SSRI use include dry mouth, nausea, nervousness, insomnia, drowsiness, weight gain or loss, dizziness, headache, and sexual response difficulties. Side effects associated with SNRIs are similar, but are less likely to include weight gain or loss and more likely to include loss of appetite and agitation. While these medications aren't addictive, discontinuing them may cause symptoms of withdrawal, including dizziness, headache, 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 release. When this reuptake is blocked or inhibited by these medications, 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 well 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, are impacted (Charney and Drevets 2002). In addition, research indicates that areas of the cortex, including the anterior cingulate cortex, are 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. (And as mentioned, some people may experience a worsening of anxiety symptoms at first.) It therefore became obvious that an increase in serotonin levels couldn't be responsible for these delayed

changes, 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 new levels of 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). In other words, new, higher levels of serotonin may somehow stimulate the 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 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 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 (see 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. Side effects such as reduced blood pressure, dizziness, breathing difficulties, nausea, cold hands or feet, tiredness, and even depression can occur with the use of beta-blockers. 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. 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 a promising 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 have 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. 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 great hope for people who suffer from anxiety. At this point, D-cycloserine hasn't been widely used in the treatment of anxiety, 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. As more of the processes underlying anxiety are illuminated by researchers, drug manufacturers will directly target these processes. New anxiety medications that facilitate the rewiring of the anxious brain may be on the horizon.

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Sample of Completed Anxiety-Provoking Situations Worksheet

A blank form for your use can be found on the next page.

Situation That Causes Anxiety	**Level of Anxiety** (1–100, low to high)	**Frequency** (per day, week, etc.)	**Triggers in the Situation**
Neighbor's dog	*70*	*once a week*	*Barking, size of dog, teeth, quick movements, jumping, thinking dog will bite me, sound of dog's tags, fence*
Flying	*100*	*twice a year*	*Packing, driving to airport, imagining crash, walking in terminal, waiting at gate, boarding, fabric of seats, taking off, turbulence, landing*
Feeling faint	*25*	*daily*	*Heights, bridges, railings, spinning, curvy road, skipping breakfast, tired, dehydrated, overheated, chemical smells, dizzy*

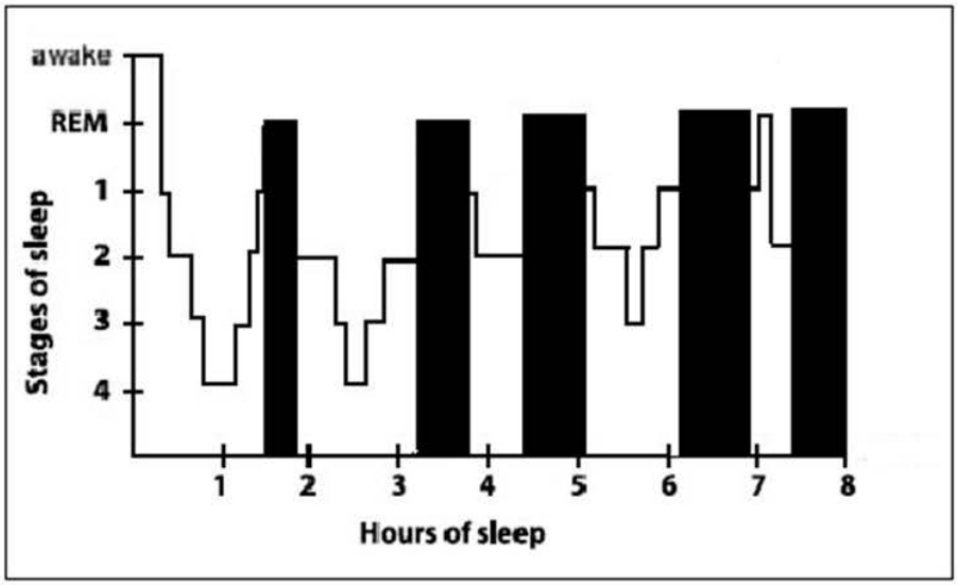
Anxiety-Provoking Situations Worksheet

Situation That Causes Anxiety	**Level of Anxiety** (1–100, low to high)	**Frequency** (per day, week, etc.)	**Triggers in the Situation**

More Sleep Will Calm Your Amygdala

(A Bonus Resource from *Rewire Your Anxious Brain*)

As we discuss in chapter 9 of our book *Rewire Your Anxious Brain*, researchers have found that when people get more sleep, the amygdala is less reactive (Yoo et al. 2007). In particular, the amygdala seems to benefit from a specific stage of sleep commonly called rapid eye movement (REM) sleep. When we sleep, we follow a specific pattern of stages, illustrated in the figure below. Each night, we cycle through different sleep stages, including REM sleep, several times in a repetitive manner. As the illustration below clearly indicates, we typically get more REM sleep (represented by the dark bars) as the night goes on, with longer and more frequent periods of REM sleep occurring in the later hours of a period of sleep.



REM sleep is the stage of sleep during which dreaming occurs; it's also a time when memories are consolidated and neurotransmitters are replenished. And REM sleep appears to have an effect on how the amygdala responds to emotional events we've encountered. There are different theories about what happens during REM sleep; one theory that might explain the changes to the amygdala

is that REM sleep helps the brain process emotional events. Whatever the reason, getting good sleep can be particularly important for people who have very reactive amygdalas. Studies show that getting sufficient sleep, and especially sufficient REM sleep, can help calm the amygdala (van der Helm et al. 2011).

When you focus on getting adequate sleep, it's important to consider *when* in the night REM sleep occurs. REM sleep occurs later in the sleep cycle and becomes more frequent as the sleep period extends. Few people realize that a long period of sleep is necessary to get into these longer stages of REM sleep. Four hours of sleep followed by an hour of wakefulness and then another four hours of sleep isn't equal to eight hours of sleep. When you return to sleep after being awake, the sleep cycles start over from the beginning, and it will take many hours to get through the entire cycle again.

Improving your sleep can have a remarkable effect on your amygdala. The best approach to improving sleep is to take a careful look at your sleeping practices and make sure that they are healthy. The following sleeping practices can really assist you in achieving a good night's sleep.

Sleep Tips

1. **Before you go to bed, practice the same relaxing rituals.** The brain is very sensitive to patterns, and if you get into the habit of repeating the same steps before bed (for example, drinking a cup of tea, washing your face, brushing your teeth, and putting on your pajamas), you'll train your brain to anticipate that sleep is coming. This will make it much easier to fall asleep.

2. **Eliminate light stimulation for at least one hour before bed.** Avoid watching television or using computers or other electronic devices that shine light into your eyes (including cell phones) before going to bed. Your brain can interpret the artificial light as daylight, making it more difficult for your brain to prepare for sleep.

3. **Exercise during the day.** Vigorous exercise isn't necessary; any type of daily exercise can help promote sleep. Just try not to schedule your exercise later in the evening, when it can be counterproductive if it's too stimulating.

4. **Establish a consistent bedtime and waking time.** Keeping a regular sleep schedule will help set your brain's clock and establish a practice that becomes a pattern of responding. It is very difficult for the brain to adjust to sleeping on a schedule that's constantly fluctuating.

5. **Avoid napping.** Any nap more than about twenty minutes long can potentially interfere with your ability to fall asleep at night, and even twenty-minute naps later in the day can be detrimental.

6. **If you have trouble falling asleep, replace activating thoughts with relaxing ones.** Focusing your thoughts on something relaxing is much more effective than trying to clear your mind. Music is helpful for some people, but others find that it doesn't prevent anxiety-igniting thoughts and therefore they need to avoid listening to music. The left hemisphere often needs to hear words to keep it from generating anxiety-igniting thoughts. Get in bed, and if you don't fall asleep quickly, read a book or listen to a podcast. You can listen to television or a video on the computer, as long as you don't watch the lighted screen in order to focus your thoughts on less activating topics. There are also many recordings on YouTube consisting of meditative exercises, relaxing nature sounds, and repetitive mantras that are ideal for this purpose. When you begin to feel that you can fall asleep, immediately turn off any lights, close your eyes, and allow yourself to sleep.

7. **If worries haunt you at bedtime, schedule a worry time during the day.** If you start worrying as soon as you get in bed, set aside at least fifteen minutes early each day for worry time. During that time, write down a list of all your worries. For each worry, write down either the best solution that you have, a note that you'll take more time to consider the solution and decide later, the name of someone you can ask for help with the situation, or that you'll live without a solution for the time being. Then fold the piece of paper and put it next to your bed to remind you that you've already worried at the appropriate time and need not do so at night.

8. **Ensure that your sleeping environment is conducive to sleep.** Your room should be dark and quiet, your bed and pillow should be comfortable, and the temperature should be agreeable. If your environment is noisy, a fan or other white noise may be helpful.

9. **Avoid caffeine, alcohol, and spicy foods in the late afternoon and evening.** All of these substances can interfere with falling asleep, staying asleep, or sleeping soundly. Even though alcohol is relaxing and can help you fall asleep, it interferes with entering the later stages of sleep, including REM sleep.

10. **Use relaxing breathing techniques to prepare for sleep.** When you get into bed, slow your breathing down and breathe more deeply. Focus on relaxing your muscles and breathing out any tension.

11. **If you can't fall asleep after thirty minutes in bed, get up and do something relaxing.** Don't remain in bed very long without falling asleep. Get up and do something calm and non-stimulating for a while, being sure to avoid computers and other light-producing screens, including cell phones. When you feel relaxed or sleepy, get back in bed. Using your bed primarily for sleep trains your brain to associate it with falling asleep.

12. **Avoid using prescription sleep aids.** Many medications that promote sleep are addictive and lose their effectiveness after a relatively short period of time. They also can cause unpleasant side effects and even abnormal behavior, such as sleepwalking or eating while sleeping! When it comes to sleep difficulties, approaches that don't rely on medications are preferable and much more helpful in the long run.

Sleep benefits the cortex as well as the amygdala, but the amygdala is especially sensitive to sleep deprivation. If you could use functional magnetic resonance imaging to see the increased level of activation in your amygdala after a night with limited sleep, you'd be amazed (Yoo et al. 2007). If you reflect on how you've felt after nights of reduced sleep, you can probably recall being more edgy or irritable. Your amygdala was likely contributing to this emotional reaction. Changing your sleep habits to ensure sufficient sleep can be very effective at reducing reactivity of the amygdala and decreasing your anxiety as a result.

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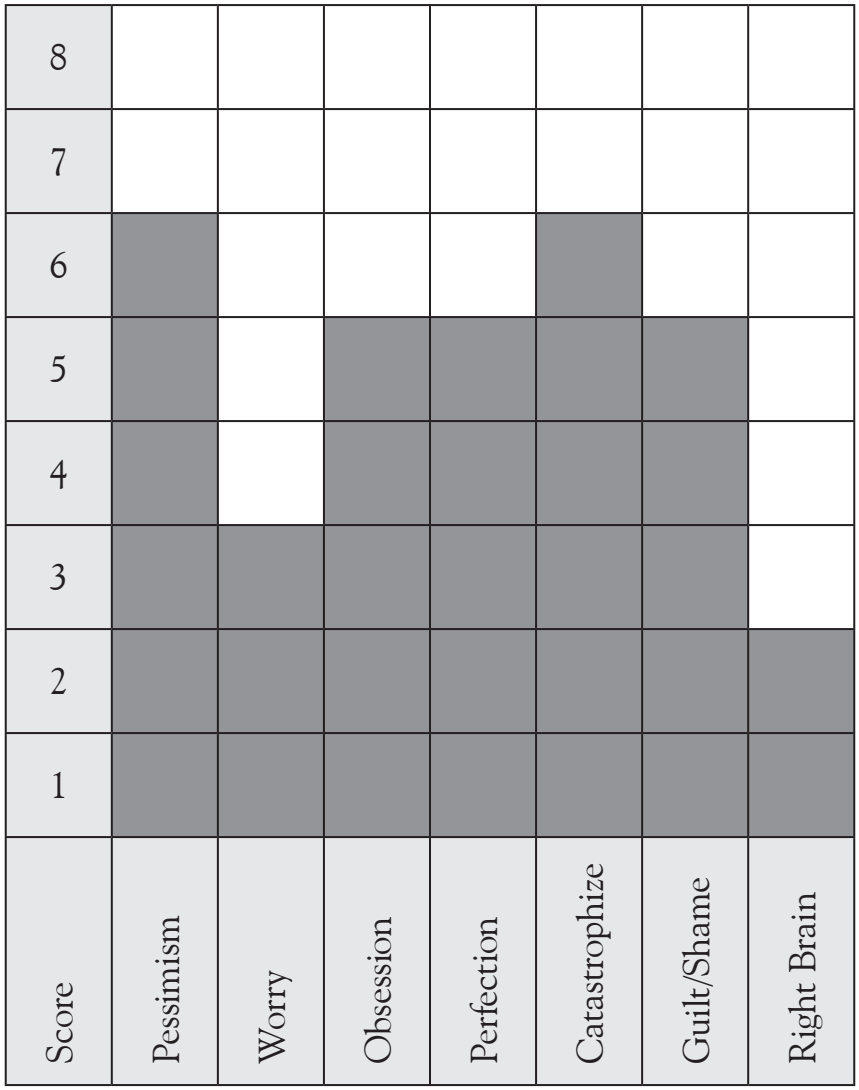
Anxiety-Igniting Thoughts Profile

After you complete the assessments in Chapter 10, this profile will allow you to graph your scores so that you can see your most frequent anxiety-igniting thoughts at a glance. Color in the boxes over each word to indicate your score on each assessment. For example, Jill received scores of 6 on Perfectionism and Catastrophize, a score of 3 on Worry, a score of 2 on Right Brain, and 5s on the remaining assessments. Note how Jill would complete the profile.

A blank profile form is on the next page of this document for your use.



Anxiety-Igniting Thoughts Profile

Score	Pessimism	Worry	Obsession	Perfection	Catastrophize	Guilt/Shame	Right Brain
8							
7							
6							
5							
4							
3							
2							
1							