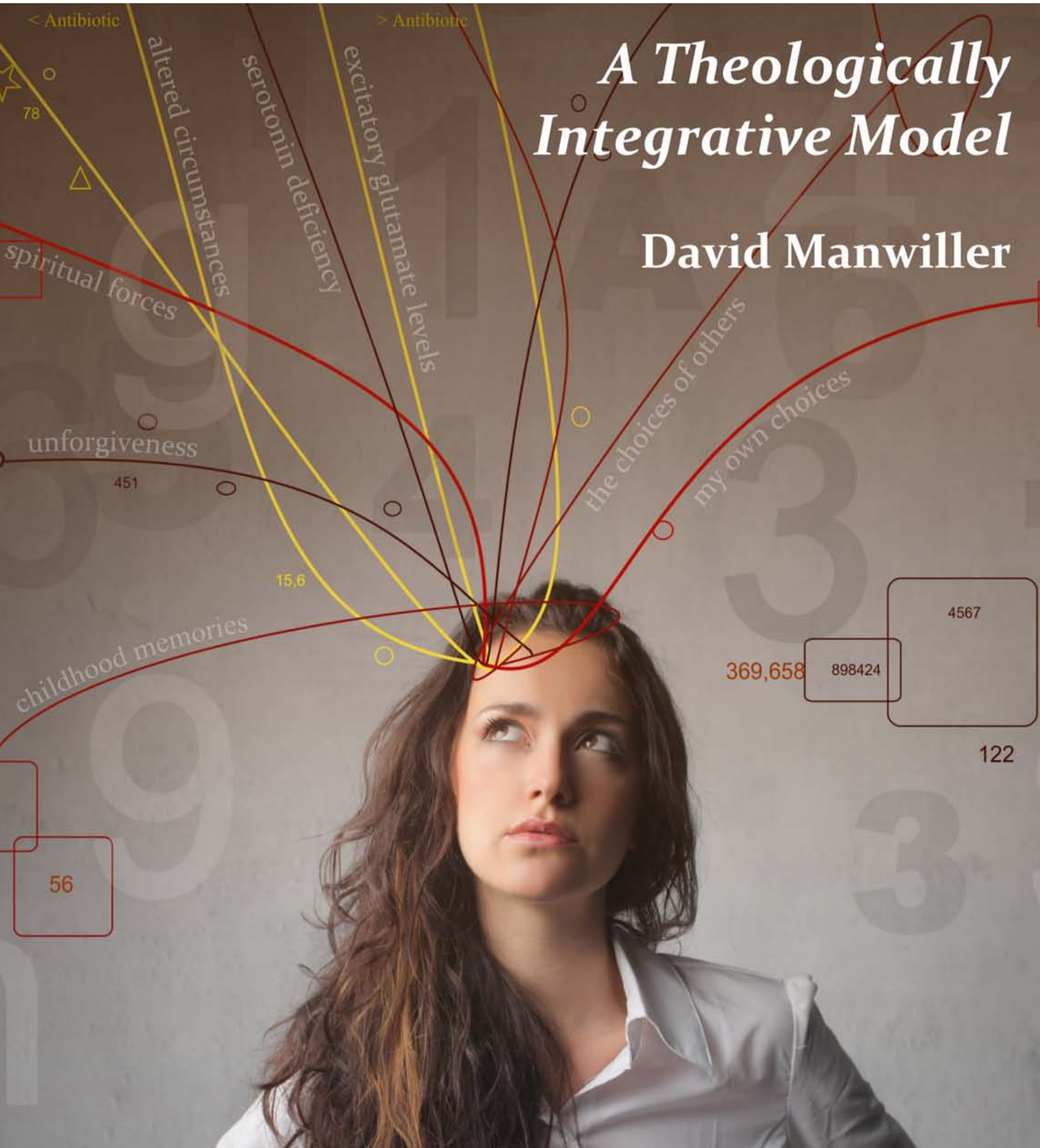
Turning Chaos into Balance

Healing Brain Chemistry & Finding Spiritual Peace



CHAPTER 1: THEOLOGY OF SUFFERING

Where Does Suffering Come From?

From a theological perspective, where does suffering come from? Theologians would answer, "The world, the flesh, and the devil" (Grudem, 1994, p. 421). Let us see how this axiom of systematic theology can be integrated with the study of neurological illness.

"The World, the Flesh, and the Devil"

Some disorders can be fundamentally outside of one's control. Narcolepsy is one example. A narcoleptic (someone who spontaneously falls asleep) experiences symptoms because he cannot produce enough hypocretin, a brain neurotransmitter (brain chemical). Presumably, Adam and Eve's neurotransmitter levels would have been perfect. But now we live in a fallen *world*, where disease and suffering take their toll.[2]

However, there are many disorders where volition, or free will, comes into play. Someone with antisocial personality disorder, for example, has more control over his actions than the narcoleptic. He will experience symptoms resulting from his antisocial choices. This is what theologians mean when they use the term "*flesh*"—sinful volition.[3]

Lastly, there are occasions when a person's symptoms may be due to overt *demonic* influence. For example, the Gerasene demoniac's insanity was due to the legion of demons controlling his thinking (Luke 8:26-39). After the demons were required to leave, Luke says the man was "in his right mind" (v. 35).

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[2] "The world" refers to suffering incurred from the fallen *physical* world. This includes physical problems in one's body, suffering caused by other physical elements, and the sinful actions of others. It does not include suffering incurred through one's own volition or demonic influence.

[3] Though perhaps confusing, the word "flesh" is not referring to the physical body. It should also be noted that the capacity for sinful volition is not only distinct from—*but was preceded by*—a fallen physical world. See Joubert (2011) for further explanation of Adam's pre-Fall ability for sinful volition and its application for understanding post-Fall hamartiology (the study of sin).

Complex Suffering

The examples above illustrate how suffering caused by the world, the flesh, or the devil, individually, can present in the human mind. But most clinical presentations are "complex"—due to a *combination* of factors. To illustrate, a teenage boy with ADHD usually has some amount of control over his aggressiveness and impatience. These behaviors, to the degree they are acted out of volition, have to be recognized as sin. A brain scan, however, would likely show that his prefrontal cortex has below average blood flow, compared to a healthy brain, thus limiting his capacity and culpability.

Also, consider a woman, mistreated and abused by relatives as a child (due to a fallen world), who now has eating disorders. It could be argued this woman would never have developed a problem had it not been for the actions of other people. Yet, despite the past sins of others, she still has a choice every day about how she eats. In these two cases, we have identified more complex situations where two domains of suffering—the world and the flesh—are both at work in creating a diagnosis.

Much more could be said about the world and the flesh, but what about demonic influence? Can all three lead to suffering in one person?

Imagine a struggling Christian man who dislikes his job and is often angry toward his family. Recently diagnosed with intermittent explosive disorder, he has a stressful career and a problem synthesizing serotonin (both results of this world). Even so, the condition is not so severe that his volition is gone. It is clear that he still has a choice when he lashes out at others (result of the flesh). Moreover, because of his continued anger and unforgiveness, the man has now opened himself to demonic attack (result of the devil).

A Closer Look at Demonology

This third source of suffering—"the Devil"—merits a section of its own, because it is often misunderstood. The Apostle Paul exhorts, "In your anger do not sin: Do not let the sun go down while you are still angry, *and do not give the devil a foothold"* (Eph. 4:26-27). As this passage indicates, a foothold for the devil can be facilitated through anger. The Greek word *topos* in v. 27, translated "foothold" in the NIV, literally means "place." More figuratively, it can mean "opportunity" or "chance" (Danker, Bauer, & Arndt, 2000). The latter interpretation is given by Hoehner (2002), "'Opportunity' gives the best sense in this text…Paul does not want believers to give the devil an opportunity by their anger" (p. 622). Arnold (2010), in his recent commentary on Ephesians, favors the more literal reading:

> Although the third clause does not begin with a causal injunction, this is the semantic function of the statement [that is, v. 26 and v. 27 are connected grammatically]. It provides a compelling reason for bringing anger under control. In particular, Paul states that by nursing anger, one can give a "place" (*topos*) to the devil. Although it is possible to take this term in the metaphorical sense of "chance" or "opportunity," it is best interpreted according to its spatial significance of "place"…Luke records Jesus as saying, "When an evil spirit comes out of a man, it goes through arid places (*topon*) seeking rest and does not find it. Then it says, 'I will return to the house I left'" (Luke 11:24). A similar usage is found in the Apocalypse: "And there was war in heaven. Michael and his angels fought against the dragon, and the dragon and his angels fought back. But he was not strong enough, and they lost their place (*topos*) in heaven (Revelation 12:7-8)…
>
> As ruler of a realm of spirits, it is unlikely that he [the devil] is personally assailing every Christian, but is assigning his spirit emissaries to do the work.
>
> By allowing anger to fester and grow, believers can surrender space to a demonic intruder (pp. 302-303).

Does sinful anger actually allow a demon to have a "place" in a Christian's body? Or does it simply give the demon a "foothold" or "opportunity" for power in his life? Semantic debate aside, it is clear that spiritual forces can exacerbate or contribute to overall suffering. Unbelievers are at even greater risk for their sin to invite the work of Satan (Eph. 2:1-2); they have no "breastplate of righteousness" (6:14).

Even a fully protected soldier is not immune from attack. The Apostle Paul himself encountered demonic opposition that caused substantial suffering (as did Job, another very righteous man). Serving God devotedly in this life will incur suffering from the world and the devil (John 15:18-19; 1 Cor. 7:5). We should be cautious, however, not to use the world and the devil as excuses for our own sin. A person's suffering could indeed be caused by demonic attack and by some elements of this world, but the largest component of all may be the result of his own choices. Some balanced, poignant insights are offered by Sproul (2007),

> The Christian is engaged in a three-front war. The Bible, replete with martial language, bears this out. The great evil trinity against which we fight is the world, the flesh, and the Devil…
>
> [Some Christians] claim to see a demon behind every bush. They don't catch colds; they are under attack by the sniffle demon. They don't have wandering eyes, but are at war with the lust demon. Often those in this camp are looking for demons behind every bush, because they can prove quite useful for excusing our sin—as Flip Wilson used to say, "The Devil made me do it."
>
> This is not the danger we face in Reformed circles. We are on the other side of the spectrum. Unlike the materialist, we do indeed believe in the demonic realm. The Bible, after all, talks about such things. But we tend to believe that demons exited the human stage at the same time that miracles ceased. Demons exist, we are willing to confess, but they have been sitting on the celestial sidelines since the apostolic age. What drives this, I'm afraid, is less a careful exegetical study of the matter, and more an embracing of the modernist worldview. We look down our noses at our brothers who pay attention to the spiritual realm not because we find such to be unbiblical, but because we find it unsophisticated. We think Martin Luther's habit of shouting at the Devil, of throwing his ink well at him, is a sign that Martin was on the psychological brink, when perhaps we ought instead to conclude that he exhibited here the same wisdom that led him to declare, "Here I stand!" It may be that Luther mined the truth that our God is a mighty fortress from the same source where he discerned that this world is with devils filled, namely, the Bible" (para. 1; 3-4).

A Theologically Integrated Model

As Sproul rightly says, we cannot embrace a modernist worldview regarding the spiritual realm. Nor can we, very well, embrace the increasingly popular, and sometimes very spiritual, postmodern approaches to psychotherapy (Shallcross, 2012). As Christians entrusted to help

those who are suffering, our model of psychopathology must be securely grounded—not based on "hollow and deceptive philosophy, which depends on human tradition" (Col. 2:8).

Does this mean there is nothing at all to learn from secular theories? No; in fact, the remaining chapters will be devoted to concepts from a secular theory called "complex systems." As we embark on this study, though, let us make sure our grounding is secure. As illustrated in the examples given in this chapter, there is no denying the physical, emotional, and spiritual realities that are able to compromise a person's psychology. We may not always be sure how much a certain disorder is of the world, the flesh, or the devil. But the point is this: *Mindfulness* of these three, and how they work together to create *complex* clinical presentations, is the most biblical and accurate way to view abnormal psychology.

Thinking reductionistically, instead of holistically, regarding a diagnosis can easily lead a clinician astray. For example, with respect to the boy's ADHD, if his impatience and aggressiveness were viewed strictly as sinful behaviors we might overlook the fact that he has reduced neurological capacity. However, to blame all his problems on neurology or other aspects of a fallen world, and not recognizing sin for what it truly is, would also be inaccurate.

A diagnostic mentality that reduces a disorder to completely physical (of the world), or to completely emotional (of the flesh), or to completely spiritual (of the devil) explanations is often insufficient. Reductionistic thinking is best replaced with an approach that sees mental health, and illness, as a complex whole.

CHAPTER 2: COMPLEX SYSTEMS THEORY

The Current Rise of Holism

Holism, in a word, is the argument I am presenting. Until recently, there was little interest in studying holism at the scholarly level except in areas of philosophy and religion. However, with the advent of complex systems theory and its derivatives (see appendix), there has now been a plethora of literature published on this topic in every discipline. Holism is increasingly gaining favor amongst the academic and applied sciences of psychology (Shallcross, 2012), neurology (Ben-Yishay & Diller, 2011), internal medicine (Hart, 2010), cybernetics (Trappl, 2008) and business mathematics (Dugsin, 2003), to name a few. The literature describes how problems occurring within complex systems are best analyzed and managed as *wholes*, rather than attempting to analyze and manage a system's components in isolation from each other (Auyang, 1999).

This interdisciplinary field of study, also called "complexity science," relies heavily on advanced mathematics and network-based modeling. The inherent complexity of this topic can lead authors in the field to become so technical that readers often lose sight of the forest for the trees. On the other hand, we do not want to adopt a superficial approach either. I will give the principles of complex systems and their application to psychopathology as clearly as I can, only looking at details when they are necessary for understanding the larger picture. A non-technical approach will be attempted as we explore two powerful concepts known as *emergence* and *dancing landscape*.

Emergence

The concept of emergence is the basis for complex systems theory. Defining this concept is not an easy task and various authors use the term differently. However, commonly accepted

examples of emergence would include such phenomena as: heartbeat, consciousness, and the very meaning produced by the words and sentences on this page. These are all examples of emergence produced by complex systems—phenomena which cannot be understood by analyzing the system's components in *isolation*.

Individual cardiac cells do not produce heartbeats, nor do individual neurons experience consciousness. Common sense tells us that heart attacks and strokes must be treated as emergent wholes instead of treating particular cells. In the same way, when considering the emergent phenomena of meaning and solving problems of interpretation, one's hermeneutic should avoid analyzing a text's component parts in isolation (Duvall & Hays, 2012; Kaneko & Tsuda, 2001). In simpler terms, one should avoid interpreting "out of context."

The emergence principle also applies to the human psyche. Attempting to interpret only one component, while ignoring the others, may produce incomplete understanding. To review, the three broad components that can impact a person's psychology are the:

- "Physical dimension" (Her neurology and physical body, the actions of others, and the physical elements of the world around her.)
- "Emotional dimension" (Her volition. This is variously described in Scripture as "mind," "heart," "spirit," or "soul."[4] This immaterial component did not exist in

[4] Though not supported by scholarly linguistic work, some popular Christian teaching further divides "spirit" and "soul" based on 1 Thessalonians 5:23: "May God himself, the God of peace, sanctify you through and through. May your whole *spirit, soul* and *body* be kept blameless at the coming of our Lord Jesus Christ." However, it seems an ontological distinction between *spirit* and *soul* is unwarranted. As Grudem (1994) points out, "The problem is even greater in Mark 12:30: 'You shall love the Lord your God with all your heart and with all your soul and with all your mind and with all your strength.' If we go on the principle that such lists of terms tell us about more parts to man, then if we also add spirit to this list (and perhaps body as well), we would have five or six parts to man! But that is certainly a false conclusion. It is far better to understand Jesus as simply piling up roughly synonymous terms for emphasis to demonstrate that we must love God with all of our being. Likewise, in 1 Thessalonians 5:23 Paul is not saying that soul and spirit are distinct entities, but simply that, whatever our immaterial part is called, he wants God to continue to sanctify us wholly" (p. 479). It should also be noted that the OT employs *nephesh* (soul) and *ruwach* (spirit) interchangeably; similarly, the NT uses *psuché* (soul) and *pneuma* (spirit) interchangeably.

Adam's physical body until it was God-breathed. It also continues to live on after the body's physical death.)

- "Spiritual dimension" (The influence of God, angels, and demons.)

In a way, this classification system is arbitrary. We could have further subdivided demonic influence as separate from the influence of God and the angels. Or we could have combined the physical and emotional dimensions into a "natural" category and contrasted it with a "supernatural" category. Furthermore, how should we classify the prayers of others? Should they go in the physical dimension or the spiritual dimension? These categories merely serve as a useful construct or framework for understanding the human psyche, just as "*the world, the flesh, and the devil*" serves as a useful axiom for describing suffering within each of these components. No matter how one chooses to classify these, one thing is clear: They are not separate or static. Each component is intimately tied to the others. In other words, they form a complex system.

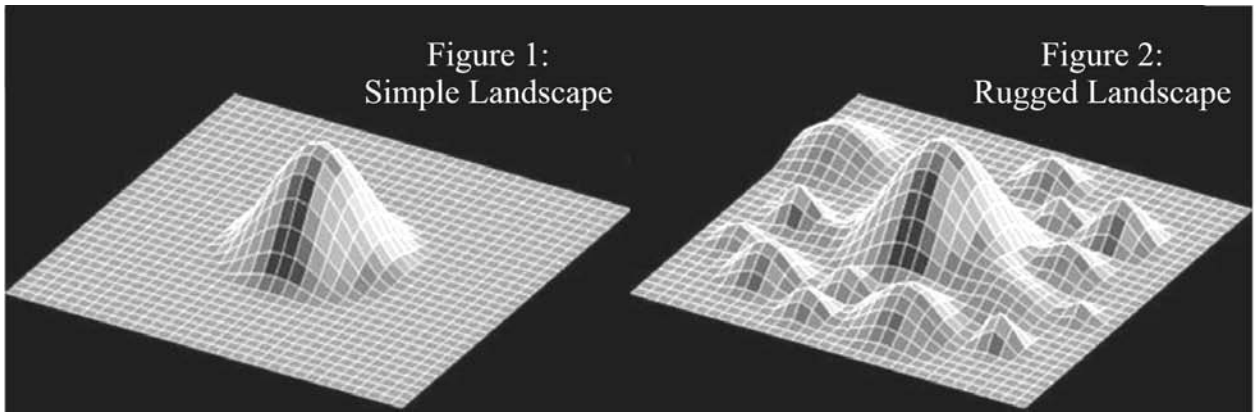
The complexity of the human psyche does not, by any means, end here. The broad components listed above are in themselves complex systems. In the next chapter, we will narrow our study to see how the *physical* dimension of mental health, itself a complex system, will also require a holistic model. However, before addressing this dimension specifically, it is necessary to look at the concept of adaptation within systems.

Adaptation

Let us see what complex systems theory says about changes within a system over time. To solve for adapting components within a system, theorists sometimes use a modeling tool called *dancing landscape*. A system's landscape is considered to dance if its components are diverse and adaptive. Landscapes that dance are contrasted with *rugged* and *simple* landscapes,

where the term “landscape” can be understood both mathematically and metaphorically (Page, 2009).

Mathematically, problems within complex systems can be graphed as the value of a function at a particular point. Higher points, called “local peaks,” represent better solutions to problems. The best solution to a problem is the highest point on the landscape, called a “global peak.” A simple landscape (a simple problem) is depicted in Figure 1, while a rugged landscape (a more complicated problem) is depicted in Figure 2.



Perhaps a more lucid way of understanding landscape is through metaphor. Let us look at Figure 1 as a mountain surrounded by flat terrain and imagine a mountain climber at the edge of the figure (I have adapted this from Page [2009]). The mountain climber’s goal is to reach the highest peak he can find. On a *simple* landscape, this is easily accomplished.

On the other hand, a *rugged* landscape poses slightly more difficulty if the global peak is not immediately in view. Then imagine a much larger landscape than Figure 2, one which stretches for miles. It might take a single mountain climber many years to find the highest point working alone and without instruments. This mountaineering expedition would go much faster with a GPS and a team of others.

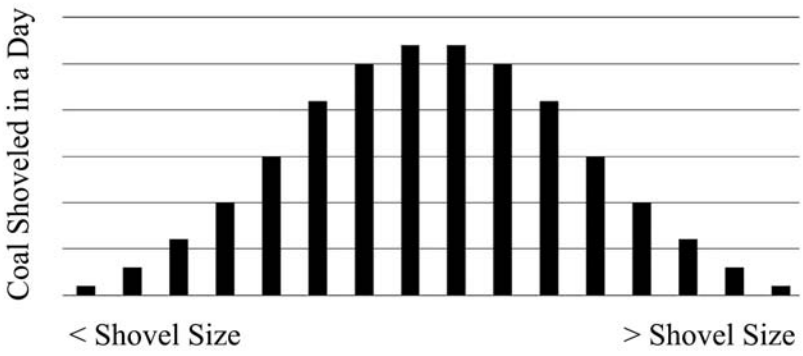
Finally, imagine one more scenario in which the peaks and valleys of this large landscape can change over time—a *dancing landscape*. At some point its global peak, which the team of climbers had worked together to reach, is no longer the highest point. Therefore, the climbers must again mobilize to conquer a new global peak on a landscape that has changed.

Simple Landscape

How do these mathematical concepts and metaphors translate into real-world problems? Regarding a simple landscape problem, Page (2009) gives the example of Fredrick Taylor and his solution to perfect shovel size.

Here is the problem: If you had the glamorous job of working on the railroad as a coal shoveler in the 1800s, you would want to be sure your shovel wasn't too big or too small. A small shovel would not let you get as much out of your work. On the other hand, if your shovel was gigantic you wouldn't be able to lift a full scoop. This *is* a problem, but it is a very simple problem to solve. It can be graphed as shown in Figure 3:

Figure 3: Representation of Perfect Shovel Size



The graph above forms a simple landscape, much like the mountain from Figure 1. A savvy mountain climber (aka "problem solver") should be able to find and conquer the global peak of this landscape without any trouble at all. In case you were interested, Taylor (1911)

found the perfect shovel size for the average man to be the volume necessary, relative to the material being shoveled, to contain 21 lbs.

Problems occurring on simple landscapes are easy to graph mathematically and good solutions can be found quickly because they lack diversity. The example above only included two simple variables—shovel size and the volume of coal shoveled in a day.

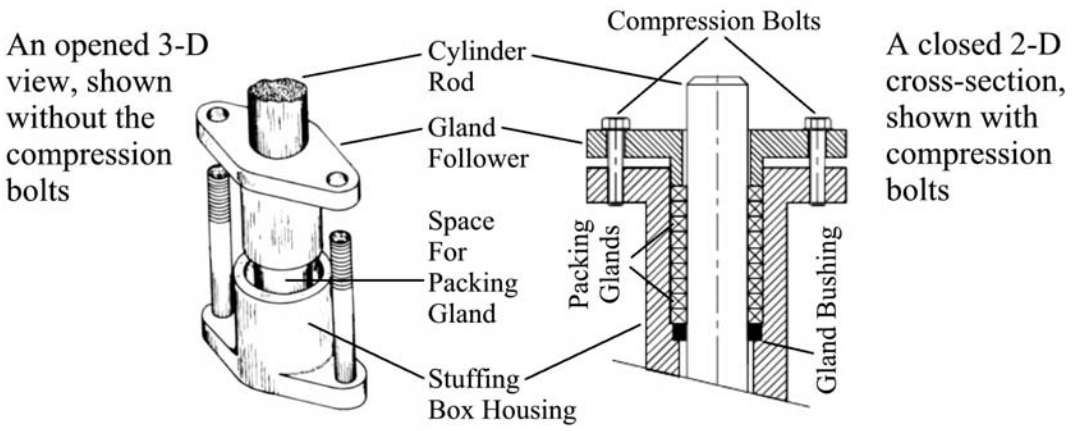
Rugged Landscape

Now we can think about a rugged landscape problem: A steam engine, into which the coal gets shoveled, contains *many* components working together to form a system. Any of these components working suboptimally could cause sudden breakdown. When this happens, there are many potential causes and, quite often, many potential solutions.

An acute engine problem is an example of a fairly large and rugged landscape. It might take an engineer several hours to diagnose and fix the problem. This is because the components of the system are diverse. However, because it is an acute problem, it is *not* a dancing landscape. Acute problems require immediate solutions, and these are not interested in adaptation.

For example, if a gasket is blown, the engineer might use an additive or apply a patch temporarily to seal the gasket. Or if the packing gland (a specific type of gasket) is wearing down, he might tighten the compression bolts on the stuffing box's housing (see Figure 4). Eventually the landscape will begin to dance (adapt) and the short-term solution will no longer be viable. But right now the train has a schedule to keep and the underlying problem will be fixed later.

Figure 4: Packing Gland Gasket & Surrounding Components



This type of compression rod seal was used on steam engine cylinders, and is still used today on modern marine drive shafts.

Dancing Landscape

Of course, the underlying problem is not the lack of an additive or a patch. The underlying problem is the broken or worn component. If it is not fixed sooner or later, the blown or wearing gasket will begin to cause inefficiency within the system. Patching and applying additives indefinitely will cause the system to become weaker and weaker. Tightening the compression bolts will not work forever. Even though acute problems can be fixed with short-term solutions, a slowly progressing problem will need a solution that takes adaptation into consideration and is graphed using dancing (adapting) landscapes.

Multidimensional Complexity

With an understanding of adaptation behind us, we can now see how multiple adapting systems can converge into larger complex systems. The health of a train does not depend solely on its engine and engineer. Its cars must be properly loaded and coupled—the conductor's job. The engine must also travel on a rail line, and at the right time—the rail traffic controller's job.

All three broad components (engine, cars, and rail line) must be present and working. Together, they form a complex whole.

To summarize, when problems arise within these systems, solutions can be mapped using complex systems theory on a landscape. Problems that involve only two components can be graphed as simple landscapes. Acute problems that involve more than two components can be graphed as rugged landscapes of various sizes. Finally, a slowly progressing problem will need a solution that takes adaptation into account and can be graphed using dancing landscapes. Higher points on a landscape indicate increasing amounts of health in a system. Lower points on a landscape indicate decreasing levels of efficiency. With increasing levels of outward zoom on a space-time continuum, all simple and rugged landscape problems (including the problem of perfect shovel size) can eventually be seen as nested within a larger, dancing landscape (Kugler, Larjo, & Harel, 2010).[5]

Mental Health—A Dancing Landscape

We can now apply these principles toward psychopathology. In many ways, the health of the human psyche is similar to the health of the train. Both systems, as a complex whole, can be constructed using three layers of multidimensional complexity (engine + cars + rail line = *train*;

[5] This approach to landscape is a combination of 1) Kugler, et al.'s (2010) work in visual formalism; 2) Page's (2009) work in complex adaptive systems; and 3) the work of Yulmetyev, Ha¨nggi, and Gafarov (2000) using time intervals. Yulmetyev, et al. studied the equations of entropy within a complex system and found they were able to use this as an information measure to solve for characteristics of multiple, interrelated components. While not using the term "landscape," they explain, "The existence of a new information measure opens up new fields for exploration of information characteristics of complex systems…Undoubtedly, detection of the frequency spectra of power of entropy for memory functions gives us new unique information about the statistical non-Markov properties [i.e. non-memoryless properties] as well as memory effects in complex systems of various nature…[such as] experimental time series for living, social, and natural complex systems (physiology, cardiology, finance, psychology…)" (pp. 6191-6192). We will heavily apply this concept of time intervals (i.e. spectra of power of entropy for memory functions) in subsequent chapters on systems biology and neuroscience.

Though not dealing primarily with time intervals, Kugler, et al. originally used something called "state charts" to model problems in software development and systems engineering. Later, their work was applied to natural systems using similar "biocharts," showing layering within complex systems.

Lastly, Page's concept of "dancing landscape" hinges on the philosophical notion of agency (volition) within a complex system, and he applies this to emergent sociological phenomena. By combining elements from these constructs into a unified model, and using an analogy to describe it, we can more quickly see their applications to our subject.

physical + emotional + spiritual = *psyche*). Each one of these layers is another complex system in itself. Furthermore, both of these systems (the train and the psyche) will experience acute and slowly progressing problems due to adapting circumstances.

Occasionally, these problems can be severe. The railroad, a once thriving industry of passenger transport in the 1800s, became outmoded with the introduction of other forms of transportation. Some train owners recovered from this blow by retooling to transport goods and raw materials, but others could not recover from the changed landscape. They decided to close down or were forced out of business (Stover, 1997).

Mental health is similarly in a continual flux caused by altering circumstances, physiological changes within our own body, spiritual forces, the actions of others, and our own actions—all of which influence each other. This could theoretically be graphed as an enormous, multidimensional, dancing landscape. When a major blow changes the landscape of our psyche, we can find ourselves in a very low valley—psychopathology. In extreme cases, psychopathology can "force a system out of business" (death) or make a person "close down" (suicide). In less severe situations the system will continue to function, but not optimally. When large negative fluctuations occur, it is necessary to view the problem holistically (the whole graph), as opposed to reductionistically (only looking at one dimension).

From a Christian understanding, treatment may include medical care to address the *physical* dimension, counsel to address the *emotional* dimension, and prayer to address the *spiritual* dimension. Even secular medical texts in recent years, of a more holistic persuasion, are recognizing the need for addressing the patient's emotional and spiritual dimensions. Dunphy, Winland-Brown, Porter, & Thomas (2007) summarize,

> A patient whom we care for may be physically healthy but the spiritual, social, and psychological dimensions may not be balanced, and therefore the patient is

> not truly healthy. It has been long determined that the whole is greater than the sum of its parts. We cannot determine someone's health status without evaluating all of these attributes…
>
> In performing a complete health assessment of each patient, the health-care provider needs to ask questions related to the person's social and dietary habits; current living and work situation environment; and feelings, beliefs, and satisfaction with his or her life as well as some relevant questions pertaining to his or her philosophical and spiritual beliefs.
>
> All of these component parts of a patient's history are as important as the physical signs and symptoms that he or she may be currently experiencing. The focus on all of these attributes of a person helps to provide a more holistic view of the person that will assist in making a more comprehensive assessment as to the current health status of the patient. The determination of health is based on the synthesis of all these parameters of health and should be incorporated into all patient assessments (pp. 19-20).

This is a tall order! Fortunately, holism does not preclude specialization. Rarely is one person qualified to address every component within a complex system. "Specialists" who care for the human psyche can include pastors, counselors, doctors, and other professionals.

Working in Partnership

Awareness between specialists, working within larger systems, is important. Confusion, at best, and cascading failures, at worst, will occur within a system when specialists are ignorant of one another's domains. What if the engineer, from the example above, had no familiarity with how to work with the rail traffic controller, conductor, or other employees at the railroad? No doubt there would be some amount of confusion and misunderstanding when problems arose on the train. Worse yet, what if the engineer did not even realize that he was working on a component that was inside a larger system?

Unfortunately, we have a mental health system filled with specialists who are often ignorant of each other and unaware that the dimension they are working on is part of a larger system. Sometimes pastors, only viewing psychopathology from the emotional and spiritual dimensions, do not recognize the physical dimension of mental health. Sometimes doctors,

viewing psychopathology only from the physical dimension, do not recognize the emotional and spiritual dimensions of mental health. Sometimes counselors, only viewing psychopathology from the emotional dimension, do not recognize the physical and spiritual dimensions of mental health.

Each specialist has a role to play. Doctors and other medical professionals make sure that a person's physical body is in working order. Pastors make sure that people are heading in the right direction spiritually. Counselors often find themselves loading, unloading and connecting emotions that have come apart.

Each component is necessary for a whole and healthy system. No matter how properly loaded and connected the cars are, they will not accomplish much with a struggling engine. Similarly, a working engine without all of its cars is not very helpful either. Nor is a working train speeding down the wrong track.

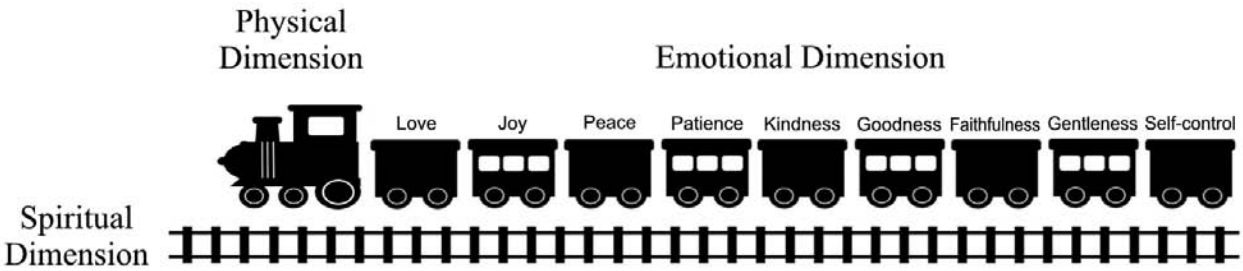


Figure 5: Multidimensional Complexity

The key lesson that can be drawn from this chapter is the need for mindfulness. As a technical psychological term, *mindfulness* is understood as a superordinate view and awareness of one's self. Specialists can encourage their parishioners, clients, or patients to become aware of their "system" as a whole. Specialists, themselves, can also practice mindfulness by becoming

aware of their function within a larger system. Those who care for the human psyche need to be aware of the system's broader components—even if they are not qualified to address them all. Each dimension needs to be working well in order for the system to function optimally.[6] Dunphy, et al. (2007) conclude,

> Optimal health is created by a balance of all of the components of health previously described: physical, psychological, and spiritual health…Optimal health promotion efforts will be achieved only through the efforts of the individual, health-care provider, and community working in partnership (p. 20).

This is a call to mental health specialists: We must work in *partnership*. Going back to our original landscape analogy—like a team of mountain climbers working together—we can find the global peak of problems more quickly if we help one another. Our competition is not with each other. It is with the spiritual, emotional, and physical components that lead to complex suffering.

In addition, we must be *mindful* of the solutions we are giving. Are the solutions designed for rugged or for dancing landscapes? We will analyze this question in the next chapter.

[6] As with most analogies, this one is imperfect. Many people go their entire lives without needing to see a counselor or a doctor for their mental health, whereas runaway trains without their conductor and engineer don't get very far. Obviously, I am not suggesting that each person requires the services of all these professionals.

CHAPTER 3: SYSTEMS BIOLOGY

One reason for the tension often found between pastors, doctors, and counselors surrounds the issue of psychopharmaceutical drugs. To understand this conflict, we can narrow our focus, at this point, to see how the physical dimension of mental health is *itself* a complex system that requires a holistic model. Until very recently, medical doctors did not receive much training along these lines. The Western medical model was originally based on a reductionistic view of systems. As explained by Ahn, Tewari, Poon, & Phillips (2006),

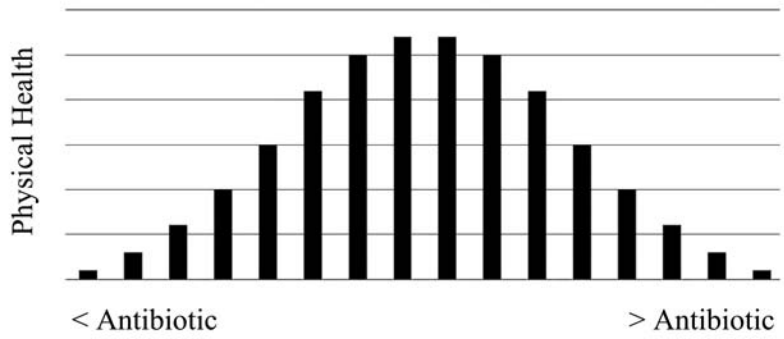
> This approach can be described as one of "divide and conquer," and it is rooted in the assumption that complex problems are solvable by dividing them into smaller, simpler, and thus more tractable units. Because the processes are "reduced" into more basic units, this approach has been termed "reductionism" and has been the predominant paradigm of science over the past two centuries. Reductionism pervades the medical sciences and affects the way we diagnose, treat, and prevent diseases. While it has been responsible for tremendous successes in modern medicine, there are limits to reductionism, and an alternative explanation must be sought to complement it.
>
> The alternative explanation that has received much recent attention, due to systems biology, is the systems perspective. Rather than dividing a complex problem into its component parts, the systems perspective appreciates the holistic and composite characteristics of a problem and evaluates the problem with the use of computational and mathematical tools…
>
> While the field of systems biology is young, it has been received with substantial enthusiasm. Many believe that, without a system-level understanding, the benefits of the genomic information cannot be fully realized. The perceived importance of this understanding is reflected in the investments made by major academic and industrial centers within the past few years (para. 1-2; 21).

Reductionistic approaches, from a systems biology perspective, will neglect at least one aspect of diversity or adaptation. The limits faced by the current medical model are usually related to the latter—adaptation. Conversely, reductionistic approaches are very capable at finding solutions to problems that do not require a high need for taking adaptation into account. This is why the Western medical model finds its most success in treating *acute* illness.

Neglecting Adaptation

To illustrate, for bacterial meningitis, antibiotics are prescribed (Chaudhuri, 2008) because they are needed to treat an acute and life-threatening infection of the brain's surrounding tissue. The antibiotic will not be effective at killing the infection unless enough is prescribed. On the other hand, massive dosages could cause the patient to experience significant side effects. The solution will be a dosage of antibiotic (Greek *anti+biōtikos*: "against life") that sufficiently destroys the lives of the bacteria without compromising the patient's own life. The problem can be graphed as a landscape:[7]

Figure 6: Representation of Proper Dosage of Antibiotic



In contrast to the landscapes depicted in Figures 1-4, this particular "mountain" was more challenging to find because it was part of a very large, rugged landscape. For the doctor, it was like trying to find the highest peak on a landscape that stretched for miles. This is because the human body has a vast number of components. The problems to be solved (in this case: headache, neck stiffness, and fever) could have been caused by many different physical factors. To verify the right mountain to conquer, fortunately the climber (the doctor) was able to use a

[7] In theory, the landscape's peak will have a definite apex. In practice, this peak is more blunted; antibiotic dosage does not require perfect calibration (Dr. D. Boyer, personal communication, 2012).

GPS (blood test or spinal tap) to identify (diagnose) the highest mountain (the meningitis bacteria).

Nevertheless, because it was an acute problem, this was not a dancing landscape. In the case of life-threatening and other acute illness, although the symptomatology observed is an emergent whole, the problem itself can be stated as the value of a function on a *rugged* landscape.

When solutions designed for rugged landscape problems are applied indefinitely to dancing landscape problems (like chronic illness), the net effect may be counterproductive. For example, long-term use of antibiotics will lead to gastrointestinal dysbiosis (a gut flora imbalance caused by the death of beneficial gut flora) and antibiotic resistance (Katz, Lynch, & Littenberg, 1996; Baxter, Ray, & Fireman, 2008). These phenomena are the result of adaptation within the system over time. Bacterial mutations within the body and the changing balance of gastrointestinal ecosystems are the unintended results of not taking adaptation into consideration.

Stated another way, adaptation requires significant time. Thus, neglecting adaptation in one's approach to acute illness is not detrimental. Acute illness (meaning rapid onset, short course, or extreme severity) is rightly viewed as a problem occurring on a landscape of small time interval. Small time intervals do not facilitate significant adaptation between components in a system (short-term use of antibiotics is unlikely to cause significant side effects). Larger time intervals, or multiple rounds of small time intervals, will facilitate significantly higher adaptation, as in the examples above (mutation and dysbiosis). Although properly viewed as a rugged landscape that will dance over the course of time, the acute problem itself can be graphed as the value of a function on a landscape that lacks the component of adaptation.

In the face of chronic or slowly progressing illness, however, the time interval of the problem is increased, which forces us to find solutions that will be effective on a continuously adapting landscape.

Neglecting Diversity

On the other hand, treatments that *try* to address problems on dancing landscapes can also err by not fully taking diversity into consideration. One of these errors is neglecting *dynamic states of equilibrium*, a homeostasis mode created by diverse components. The result is intervening when problems may actually be nonexistent. One example of this is the growing concern that increasing use of blood pressure medication is not actually decreasing risk of coronary heart disease in many patients. Ahn, et al. (2006) explain,

> Because reductionism often disregards the dynamic interactions between parts, the system is often depicted as a collection of static components. Consequently, emphasis is placed on static stability/normal ranges and not on dynamic stable states, such as oscillatory or chaotic (seemingly random but deterministic) behavior. Circadian rhythms are an example of oscillatory behavior, and complex heart rate variability is an example of chaotic behavior. Failure to include these dynamic states in the homeostasis model may lead to treatments that are either ineffective or even detrimental.
>
> Since disease cannot always be predicted with certainty, health professionals must identify and modify risk factors. The common, unidimensional, "one-risk factor to one-disease" approach used in medical epidemiology, however, has certain limitations.
>
> An example is hypertension, a known risk factor for coronary heart disease. Guidelines suggest pharmacological and lifestyle treatment for individuals with systolic blood pressure greater than 140. This strategy is supported by evidence from the Framingham Study, which showed that men between 35 and 64 years of age with systolic blood pressures greater than 140 were twice as likely to develop heart disease as compared to individuals with systolic blood pressure less than 140. However, given that nearly 70% of the American population is not affected by hypertension, up to 30% of coronary artery disease develops in individuals with normal blood pressure. Conceivably, a large number of people at small risk may give rise to more cases of disease than a small number of people at high risk. This observation is termed the prevention paradox.
>
> To capture these missed cardiac events, the natural recourse is to progressively lower the blood pressure threshold for treatment. Consequently, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of

> High Blood Pressure lowered its initial diastolic blood pressure threshold of 105 in 1977 to 90 in 1980, to 85 (for high normal) in 1992, and to 80 (for prehypertension) in 2003. The cost of such a strategy is the unnecessary treatment of individuals who wouldn't have developed coronary disease in the first place. This problem originates from the constraints imposed by a one-risk to one-disease analysis and the inability to work with multiple risk factors and calculate their collective influences. If a more multidimensional analytical method were used, then more precise risk projections for individuals could be devised ("Current Medical Science" section, para. 6-9).

Application to Psychopathology

These principles, regarding diversity and adaptation, can also be applied to psychopathology and to decisions regarding the use of psychotropic medication. Is the psychopathology in question of rapid onset, a short course, extreme severity, or a meaningful indicator of future acute pathology? Or is the psychopathology of slow onset, chronic, low severity, or simply the product of dynamic states of equilibrium that cannot be accounted for using unidimensional assessments?

As in the antibiotic example above, adaptation must be taken into account when long-term use of psychotropic medication is considered. What long-term effects will this medication have? Will neurotransmitter imbalances become resistant to the corrective psychopharmaceutical over time? From a holistic approach, taking diversity and adaptation into consideration, these questions need to be asked.

Sometimes strategies that work for the short-term will not work well for the long-term. Though it works well for the short-term, continuing to apply additives and patches to a blown gasket will cause the system to become increasingly weaker. Recall that tightening compression bolts on a gasket will not work forever. Eventually the underlying problem needs to be addressed (new packing gland needs to be installed).

Though politically incorrect, it is interesting that we sometimes speak of those with mental disorders as ones who have "blown a gasket." What do we mean by this? Simply put,

something is not functioning correctly in the person's system. Short-term psychopharmaceutical solutions can often be applied temporarily without significant side effects. In fact, such measures may be required indefinitely if the system is severely damaged. However, no matter how damaged the system, it is still wise to address the underlying neurology and retool if the patient is willing.

System Retooling

Retooling is never easy and often takes longer than psychopharmaceuticals. It is almost always easier and quicker to apply short-term fixes. However, just as a train's engine sometimes requires obtaining raw material to manufacture new gaskets, sometimes an individual's body requires the raw material to manufacture new neurotransmitters. This may involve dietary changes, neurosubstrate loading, and natural methods of neuronal enzyme modulation as opposed to pharmaceutical methods of reuptake inhibition and receptor modification (agonists and antagonists). These will be covered in detail over the next three chapters, as we examine the complex psychoneuroimmunological system.

Compared to macroscopic problems, mapping the landscape of neurotransmitter imbalances is often quite difficult due to the microscopic components. However, we have a tool available now that greatly aids in this process. We will review this tool in the next chapter, as we look at recent advances in neurotransmitter analysis.

CHAPTER 4: RECENT DEVELOPMENTS IN NEUROTRANSMITTER ANALYSIS

Basic Neuroanatomy

The nervous system consists of two main divisions: the central nervous system (brain and spinal cord) and the peripheral nervous system (nerves outside the brain and spinal cord). The central nervous system receives input about the body's internal and external environment from the peripheral nervous system. The peripheral can further be dived into two categories: somatic and autonomic. The autonomic regulates all our visceral functions: heart rate, metabolism, sexual arousal, perspiration rate, pupil dilation, etc. (things, to some degree, that we can't control). The autonomic can further be divided into the sympathetic and parasympathetic branches. The sympathetic mobilizes energy and is sometimes referred to as the "fight or flight" response. The other branch, the parasympathetic, acts to conserve energy and is sometimes called the "rest and digest" response (Sherwood, 2013).

How do the various components of this complex system communicate with each other? Signals are transmitted by specialized cells called neurons. Neurons, in turn, communicate with each other via chemicals called neurotransmitters. The neurotransmitters are released from their storage vesicles in a presynaptic neuron, into a space called the synapse, before being absorbed by a postsynaptic neuron's membrane. It is this transmission, at the microscopic level, that facilitates communication within the nervous system as a whole.

Applying Emergence to Neurotransmitter Values & Symptomatology

It has long been known that neurotransmitter imbalances accompany psychopathology. However, which specific neurotransmitters are out of balance? The science of psychiatry has historically been a guessing game concerning which neurotransmitters are deficient or excessive. Unlike any other medical specialty, most psychiatrists do not run tests on the system they are

treating. This is akin to the mountain climber trying to find the highest point on a vast landscape without a GPS or other surveying tools. Like a climber who only eyeballs the landscape needing to be conquered, a psychiatrist who guesses at neurotransmitter values based on symptomatology alone is more easily led astray. This is because symptomatology is emergent—it can be created by diverse components.

Stated another way, diverse neurotransmitter imbalances can result in the same symptomatology. For example, the symptomatology of depression could be caused by excessive norepinephrine and cortisol (Hughes, Watkins, Blumenthal, Kuhn, & Sherwood, 2004), deficient serotonin (aan het Rot, Mathew, & Charney, 2009), or imbalances in the glutamatergic system (Palucha, Brański, Lenda, & Pilc, 2010). Three different people, all presenting depression, could have different imbalances.

How do researchers determine these correlations between symptomatology and neurotransmitter values? They use a test called *neurotransmitter analysis*. There are several such tests, some of which are very expensive and some that are not very effective. However, there is one test that shows much promise for clinical utility. Let us review these analysis methods.

Neurotransmitter Analysis

Neurotransmitters are present in several biological substances including urine, blood, and cerebral spinal fluid. However, collections of blood and cerebral spinal fluid are only a measurement of what is present at the moment of collection. These methods often lead to unpredictably exaggerated values. The stressful nature of the procedure spikes neurotransmitter values in some patients (Nigrovic, McQueen, & Neuman, 2007). As a result, there is, as of yet, no established clinically relevant lab ranges for these fluids (Okumura, Nakajima, Matsuoka, & Takamatsu, 1997). Urinary measurement, on the other hand, is a non-invasive collection

procedure, a sample that is representative of a 2-3 hr. time interval, and now has established, clinically relevant lab ranges (NeuroScience, 2012).

Even though urinary testing is not a direct measure of central nervous system (CNS) activity, as cerebral spinal fluid is, the literature shows that an increasing number of researchers are favoring its usage. Concerning dopamine, Cohrs, et al. (2004) explain,

> Although dopamine and its metabolites excreted in the urine could perhaps come from sources other than the central nervous system, findings of other studies support the assumption that reduced excretion of urinary dopamine indicates a decreased activity of the central dopaminergic system (p. 164).

It is becoming clear that transport mechanisms exist which shuttle intact neurotransmitters from the CNS to the peripheral nervous system (Hawkins, O'Kane, Simpson, & Viña, 2006). These intact neurotransmitters are eventually expelled into the urine via two methods called glomerular filtration and renal tubular secretion (Gründemann, et al., 1998; Marc, Ailts, Campeau, Bull, & Olson, 2011).[8]

This relationship between urinary neurotransmitter levels to CNS neurotransmitter levels was demonstrated in a 2004 study authored by Lynn-Bullock, Welshhans, Pallas, & Katz,

[8] This is another example of a complex system into which adaptation must be taken into account. Marc, Ailts, Campeau, Bull, & Olson (2011) explain, "Circulating neurotransmitters are filtered from the blood by nephrons, the functional units in the kidneys, and subsequently excreted in the urine (Moleman et al., 1992). Studies have identified the presence of neurotransmitter transport molecules on nephrons that move neurotransmitters from the extracellular space to abolish their biological actions and actively excrete them in the urine (Amara and Kuhar, 1993; Grundemann et al., 1998, 1997; Chen et al., 2004; Hayer-Zillgen et al., 2002; Kopp et al., 1983). Among these, the organic cation transporters (OCTs) are important facilitators of electrogenic uptake of small cations such as drugs, xenobiotics, and endogenous compounds (choline, DA, NE, E, serotonin, histamine, and tyramine) from the circulation, and are present in proximal convoluted tubules of the nephrons (Grundemann et al., 1998; Karbach et al., 2000). A notable property of OCTs is the concentration dependent reversibility of the transport direction thereby facilitating the bidirectional transport of organic cations (Busch et al., 1998; Gorboulev et al., 1997; Kekuda et al., 1998; Koepsell et al., 1999)" (p. 637).

Because of this, it seems there is bidirectional adaptation of neurotransmitters into and out of the kidney. So, if concentrations are higher in the urine than in the bloodstream, neurotransmitters will be taken back into the blood from the urine; and vice versa. Perhaps, in some individuals, these transporters may not function properly (due to heavy metals, etc.). However, if an individual's kidneys are working properly, the urine will be a good marker because it will parallel neurotransmitter levels in other areas of the body, including the CNS and enteric (gastrointestinal) nervous system (Dr. Y. Berry, personal communication, 2012).

> We found that the time course of changes in 5-HTP [serotonin precursor], 5-HT [serotonin], and 5-HIAA [serotonin metabolite] in the urine mirrored the time course of immunoreactivity in the SNC [substantia nigra pars compacta, a midbrain structure]. These metabolites increased rapidly and returned to baseline values within 24 h (p. 137).

Having established the sensitivity of urinary testing to CNS neurotransmitter activity, let us now consider its specificity. Whereas *sensitivity* asks the question, "Does the test measure what it claims to measure?" and evaluates the proportion of actual positives which are correctly identified, *specificity* asks the question, "How well does the test measure what it claims to measure?" and evaluates the proportion of negatives which are correctly identified.

The specificity of testing results depends on which analysis method is used. In the short history of neurotransmitter analysis (about 60 years), several methods have been used including colorimetric and fluorescence-based measurement, which both lacked specificity (Kagedal and Goldstein, 1988). As the technology of urinary analysis progressed, a method known as high-performance liquid chromatography (HPLC) came to be the favored approach. It offers increased specificity, but is often time-consuming and significantly more expensive than colorimetric and fluorescence-based measurement (Westermann, Hubl, Kaiser, & Salewski, 2002).

ELISA Technology

Enzyme-linked-immunosorbent assay (ELISA) technology has combined the advantages of high throughput, reasonable cost, and a high degree of sensitivity and specificity.[9]

[9] ELISA works by coating a microplate (a flat plate with multiple "wells," used as small test tubes) with an antigen. A specific amount of urine is then added to the microplate. The urine contains neurotransmitters, as well as various other proteins. Once the urine is in the microplate, an antibody—specific to the neurotransmitter of interest—is added. This antibody will bind to the neurotransmitters that are floating generally in the plate, and also to the neurotransmitters coated on the plate. The test is only interested in detecting the amount of bound antibody to the latter—those that are coated on the plate. To detect these antibodies, a second antibody is added to the microplate. This antibody recognizes the first antibody that was added. A chelometric method (not to be confused with colorimetric) is used for calculating the specific amount of bound antibody. Higher levels of bound antibodies represent lower levels of neurotransmitters in the urine. This is because fewer antibodies became bound to the neurotransmitter in question floating in the microplate (Huisman, Wynveen, Nichkova, & Kellermann, 2010).

Consequently, ELISA is rapidly becoming the preferred method of both academic and clinical neurotransmitter testing (Francis, Pickerodt, Salewski, Boemke, & Hohne, 2010).

ELISA's urinary neurotransmitter specificity was validated in 2010 by Huisman, Wynveen, & Setter: "Antibodies displayed high specificity…[to the specific neurotransmitters in question], but not to closely related conjugated metabolites, precursors, pharmaceuticals, agonists, antagonists, or free neuro-active haptens" (p. 1). For example, when dopamine was measured in this study, sequentially diluted solutions were added to an assay of other similar neurotransmitters (TG-dopamine, BSA-DOPAC, TG-epinephrine, TG-norepinephrine, TG-glycine, and TG-ethanolamine) with no cross-reactivity.

In other words, the test *correctly* did not measure the molecules it was hypothesized not to measure. ELISA's specificity was also validated in 2010 by another study showing intra-assay precision rates between 3.9% and 6.5% CV (coefficient of variance), well within the accepted limit of 20% for immunoassay reliability. Inter-assay reproducibility was also very precise, with CVs between 5.1% and 9.2% (Huisman, Wynveen, Nichkova, & Kellermann, 2010).

Having addressed the analytical validity (sensitivity and specificity) of ELISA urinary neurotransmitter testing, we must also consider its *clinical* validity. We must look at how an individual patient's neurotransmitters vary over time. Will a person's levels be fairly consistent from one day to the next? If they fluctuate too dramatically, there would be little point in testing it.

A recent study using *Pharmasan Labs* involved 66 individuals who collected two urine samples ranging from 3 days to 3 weeks between collections (NeuroScience, 2012). The purpose of the study was to determine the degree of variance between individual baseline urinary neurotransmitter measurements over selected timeframes. A paired t-test for epinephrine

excretion consistency found a p-value of 0.5373, indicating no statistical difference between the two collection sample values. Similarly, a paired t-test for serotonin excretion consistency found a p-value of 0.9047 (anything above 0.5 shows no statistical difference). In basic terms, none of the test subjects had significant fluctuations in neurotransmitter levels—at least over the course of 3 weeks. It seems that urinary neurotransmitter levels are relatively stable over time.

Diagnostic Tool or Functional Biomarker?

Having demonstrated the sensitivity, specificity, and clinical validity of ELISA urinary neurotransmitter testing, the *diagnostic* capacity of this test remains open to question. Further research should be conducted on the correlation between CNS neurotransmitter values to symptomatology and whole-body neurotransmitter values to symptomatology. Recall that urinary testing gives whole-body neurotransmitter values as opposed to strictly CNS values.

ELISA urinary neurotransmitter testing may be best understood as a functional biomarker. Atkinson, et al. (2001) define a biomarker as "a characteristic that is objectively measured as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" (Definitions section, para. 2). Truly diagnostic biomarkers directly test for disease (e.g. a throat culture for strep infection). *Functional* biomarkers, on the other hand, are indicators of normal biologic processes (cholesterol, vitamin D, etc.). Kahane (2009) explains further,

> Overall, urinary neurotransmitter analysis can be a useful tool in any clinical practice dealing with psychiatric disorders. Clearly, research supports the clinical relevance of urinary monoamine measurements, and with the advent of improved laboratory techniques, the cost of the testing has significantly decreased along with the time it takes to run the laboratory analysis. In addition, other neurotransmitters such as glutamate, gamma-aminobutyric acid (GABA), histamine, glycine, and taurine are being measured with high specificity and selectivity. If we consider the established criteria required for a biomarker to correspond to or indicate psychiatric symptoms, urinary neurotransmitter analysis meets these necessary requirements. It is cost-effective, timely, non-invasive (to

> ensure patient compliance), and can easily be incorporated into any clinical practice. Objectivity is essential to treating patients with psychiatric disorders. Medical history and DSM-IV criteria may suffice for the diagnosis of psychiatric disorders (Maj et al. 1999; Maj et al. 2000); however, the heterogeneity of patient biochemistry can decrease successful treatment outcome (Schwarz and Bahn 2008). Neuropsychiatric biomarkers may aid in determining successful treatment regimens based on patient biochemistry rather than simply relying on standard diagnostic protocols (p. 71).

As discussed earlier regarding the functional biomarker of hypertension (see pp. 25-26), these values cannot be unidimensionally applied to current or potential pathology states (whereas diagnostic tests can be, to a greater degree). ELISA testing should be understood appropriately as a functional biomarker, taking dynamic states of equilibrium into consideration. Even so, such testing can still provide significant clinical direction for neurotransmitter modification. Testing provides more accuracy to clinicians when assessing neurotransmitter deficiencies and excesses. Testing also provides *patients* with tangible proof of pathology and incentive for complying with therapeutic interventions. Finally, periodic testing provides a monitor of intervention effectiveness. Ailts, J., Ailts, D., & Bull (2007) conclude,

> The current body of literature provides evidence that urinary neurotransmitter testing has a place in clinical practice as a biomarker of nervous system function. Studies have demonstrated intact neurotransmitter transport out of the CNS, into the periphery, via blood-brain barrier transporters. Renal filtration of neurotransmitters via specific transporters is well-documented. Researchers have provided examples of urinary neurotransmitter measurements that correlate with CNS tissue concentrations. Lastly, a growing body of evidence exists that associates urinary neurotransmitter output with various clinical conditions, correlates values with therapeutic effectiveness, and allows clinicians to make more informed decisions.
>
> Questions surrounding the source of neurotransmitters in the urine become irrelevant in light of the correlations between urinary excretion and various conditions. The studies cited offer a compelling argument that urinary neurotransmitter testing improves the ability of a clinician to make an informed decision, based on empirical evidence, in first line therapeutic choices that will improve outcomes (p. 5).

Just as GPS technology slowly improved during the twentieth century and became more widely available, tests for assessing neurotransmitter imbalance have slowly improved and are no longer limited to the academic realm. With the introduction of ELISA technology, and the growing body of research showing the clinical utility of urinary testing, it will not be very long before such testing is widely used by mental health professionals.

However, diagnosis is only the tip of the iceberg. The real challenge lies in finding effective treatments for neurotransmitter *modification*.

CHAPTER 5: PSYCHOPHARMACOLOGICAL AGENTS AND MECHANISMS OF ACTION

The Problem to be Solved

Having discovered the global peak on a landscape (mathematically, or in real life), this does not mean we are done solving the problem. Once we have surveyed the patient's landscape with our GPS (neurotransmitter testing), how are we going to climb to the global peak? Many psychopharmaceuticals are remarkably effective. However, the problem is that if a process we use to scale the landscape is too "heavy," it may change the very landscape itself. Climbing to the highest point on a landscape for the short-term, only to find that in the long run you are at a lower place than before, is a self-defeating process. For example, concerning antidepressants, Jackson (2005) finds that,

> Antidepressants have also been linked to a variety of adaptations which may be chronically pathogenic. These long term effects include changes in gene expression, changes in cell function and structure, and changes in the homeostasis and allostatic capacities of the neuroendocrine system…A significant body of research suggest that antidepressants may reduce the long term capacity of the brain to autoregulate (self-regulate) neurotransmitter systems (pp. 84-85).

The pathology of depression has been researched for many years. Many different genetic abnormalities, combined with environmental factors, will accelerate neurotransmitter turnover. It is this accelerated turnover that eventually causes deficiency. In optimal mental health, synapses are populated and storage vesicles in presynaptic neurons are full. But if the body cannot replenish its storage vesicles, symptoms will begin to arise (Bymaster, McNamara, & Tran, 2003).

When evaluating someone's depression, we must be careful not to view the problem reductionistically. She may not necessarily have a problem with sin or demonic attack. She could primarily be suffering from genetic weakness combined with other physical factors. Certainly,

prayer is still indicated when the root cause of suffering is physical. This seems to be the thrust of 2 Chronicles 16:12, regarding King Asa: “Though his disease was severe, even in his illness he did not seek help from the Lord, but only from the physicians…Asa died and rested with his fathers.” However, this passage does not preclude the use of substances for healing. Otherwise, why would Paul have recommended to Timothy, “Stop drinking only water, and use a little wine because of your stomach and your frequent illnesses”? (1 Tim. 5:23). From a physical perspective, how can we heal a person with depleted neurotransmitter levels?

Solution #1: Reuptake Inhibitors

Commonly used drugs to address symptoms that result from neurotransmitter depletion are *reuptake inhibitors*. Also known as transporter blockers, these drugs are intended to increase synaptic levels of neurotransmitters by inhibiting their reuptake back into presynaptic neurons.

SSRIs (selective serotonin reuptake inhibitors) affect the reuptake of serotonin, and include trade names like Paxil and Celexa. SNRIs (serotonin-norepinephrine reuptake inhibitors), such as Effexor and Cymbalta, affect both the reuptake of serotonin and norephinephrine. NDRIs (norepinephrine-dopamine reuptake inhibitors), such as Survector and Wellbutrin, affect both the reuptake of norepinephrine and dopamine, and so on. Regarding a non-pharmaceutical agent of reuptake inhibition, *Hypericum perforatum* (St. John’s Wort) contains hyperforin and adhyperforin, which are wide-spectrum inhibitors of all the neurotransmitters listed above (Chatterjee, Bhattacharya, Wonnemann, Singer, & Müller, 1998). The effect of the recreational drug, cocaine, is also a potent example of reuptake inhibition on the brain.

The use of reuptake inhibitors works well for the short-term. However, long-term use of these agents will eventually lead to further depletion if storage vesicles are not replenished. The need to continually increase inhibitor dosage, and eventual resistance to medications, is the result

of not addressing the underlying deficiency. This is because of *allostatic load*, the physiological consequences of chronic exposure to fluctuating or heightened neuroendocrine responses, over the course of time (Taylor, 2009). As explained by Jackson (2005),

> A growing body of research supports the hypothesis that antidepressants worsen the chronicity, if not severity, of depressive features in many subjects. One unintended consequence of pharmacotherapy appears to be the induction of protracted allostatic load (i.e. long-lasting changes in cell receptor function, effector system activity [activity of diverse molecules that, when bound to an allosteric site of an enzyme, cause either an increase or decrease in activity], and gene expression). These maladaptive responses contribute to the persistence of minor symptoms, more sustained episodes of illness, and more frequent relapses…
>
> A British team of researchers investigated the long term outcomes of 115 patients initially evaluated within 6 months of the onset or relapse of a depressive episode. After a mean interval of four months, the patients were re-evaluated for their response to treatment. At the start of the trial, 33% of the participants were experiencing a first episode of major depression, while 67% were experiencing a relapse. Recovery rates for both groups varied according to treatment…Of 44 patients who began the study in an unmedicated condition, 16 received antidepressants; 28 received no drugs or alternative medical (non-antidepressant) therapies. Of the patients who received antidepressants, 30% recovered. Of the patients who did *not* receive antidepressants, 50% recovered. Even after controlling for treatment compliance, and after controlling for the severity, duration, and type of depression (e.g. endogenous or neurotic), antidepressants were still associated with the worst clinical results (pp. 109-110).

Examples of alternative medical therapies (e.g. neurosubstrate loading) will be reviewed shortly. First, we will consider another common psychopharmaceutical mechanism of action.

Solution #2: Receptor Modification

Sometimes a deficiency of neurotransmitters is not the problem. The problem may be an *excessive* level of neurotransmitter activity. Receptor modification (of the postsynaptic neuron) involves the mimicry, enhancement, or blocking of the neurotransmitter binding process. Agents in this class include agonists and antagonists.

Antagonists (from the Greek *antagonistēs*: “opponent”), after binding to a receptor, do not provoke a biological response themselves, but will “oppose” neurotransmitters from binding and having *their* effect. Pharmaceuticals include histamine antagonists, such as Avanza (used for depression) and Norflex (used to treat Parkinson’s); serotonin antagonists, such as Sandomigran (used for recurring migraines) and Periactin (used for nightmares related to PTSD); dopamine antagonists, such as Serentil (used for schizophrenia) and Motilium (to control nausea), and hundreds of others. Examples of non-pharmaceutical antagonists include L-theanine (a glutamate antagonist found in green tea) and the PEA receptor antagonist 4-amino-3-phenylbutyric acid (Kimura, Ozeki, Juneja, & Ohira, 2006; Shulgina, 1986).

An agonist (from the Greek *agōnistēs*: “champion”) produces the opposite effect of an antagonist. Whereas antagonists stop something from happening, agonists make something happen. They usually mimic neurotransmitter activity and bind to specific receptors, resulting in an action potential that is similar to the neurotransmitter it is mimicking. Other agonists work by enhancing the effect of neurotransmitters, resulting in an amplified effect that is greater than either component could achieve on its own. Natural examples of such agonists would include supplements like taurine and herbal extracts of valerian (GABA agonists). Pharmaceutical GABA agonists include benzodiazepines, such as Xanax (used for panic and other anxiety disorders) and Klonopin (also used anxiolytically, as well as for its anticonvulsant and hypnotic properties).

Antipsychotic drugs come in both flavors—agonists and antagonists—and are now the best-selling class of any pharmaceutical in America, generating an annual revenue of $14.6 billion (Wilson, 2010). No longer are we reserving these drugs for the treatment of psychosis; they are increasingly being used in the management of non-psychotic disorders.

When weighing the impact of long-term use of psychotropic medication, we must recall how adaptation works within systems and how this applies to the brain's neuroplasticity (ability to change). Concerning antipsychotics,

> No discussion of antipsychotic effects would be complete without mentioning the *structural changes* which accompany prolonged treatment. As neuroscientists have only recently emphasized, drug therapies alter not only the function [communication via neurotransmitters] but also the *anatomy*…A substantial volume of research supports the concern that antipsychotic medications are potentially very toxic to the brain.
>
> Animal research has permitted the manipulation and observation of drug-induced changes in neuroanatomy, without the confounding influence of pre-existing neuropsychiatric conditions. Based upon cellular analyses of tissue samples from monkeys and rats, antipsychotics have repeatedly shown to alter the size, density, and properties of the neurons and glia. Following chronic exposure to neuroleptics [antipsychotics], rat brains have shown consistent reductions in neuronal density within the striatum (due to neuronal loss or striatal enlargement), as well as alterations in the structure and properties of synapses within the striatum and the frontal cortex. Some, but not all, of these changes have persisted even after medication consumption stopped. While fewer studies have been conducted in primates, architectural changes have been noted there, as well. In a study of rhesus monkeys which examined cellular changes after six months of exposure to antipsychotic drugs (typical and atypical), glial cells were found to proliferate, and the prefrontal cortex became significantly enlarged…
>
> In what may be the only published [human] study to compare brain tissue from medicated and unmedicated subjects, Jellinger reported the neuropathological findings of 56 individuals who had been diagnosed with schizophrenia. Post-mortem analyses reveled significant enlargement and scarring in the caudate of the chronically neuroleptized (89% with gliosis and swelling in large neurons) versus 4% of the subjects who had avoided treatment with antipsychotic drugs (Jackson, 2005, pp. 179-181).

Solution #3: Neurosubstrate Loading

By far the safest, and potentially most curative, therapeutic method of psychopharmacological action is through the use of specific amino acids as precursors for neurotransmitter synthesis. Agents that fall within this category can usually be obtained without a prescription.

Most of the primary neurotransmitters in the CNS must be synthesized from essential amino acids ingested in the diet; this is why they are called “essential.” In the absence of either sufficient dietary intake or absorption of these amino acids, substrate loading via supplementation can be employed to enhance the synthesis of specific neurotransmitters. In this process, orally ingested amino acid substrate is absorbed into circulation, shuttled across the blood-brain barrier via various transport mechanisms, and diffuses into neurons for use. Inside the neurons, enzymes facilitate the conversion of amino acids into active neurotransmitters (NeuroScience, 2012).

Commonly employed substrates to enhance synthesis of their respective neurotransmitters include the use of tryptophan and 5-HTP to serotonin (for sleep disorders, eating disorders, depression, situational anxiety, OCD, etc.); and tyrosine and L-dopa to dopamine (for addiction, Parkinson’s, etc.), to name just a few (Braverman, 2004). Regarding Parkinson’s, one pharmaceutical substrate loading agent is Levadopa—simply a purified form of L-dopa. The safety and efficacy of substrate loading, especially using naturally derived substrate, has been repeatedly demonstrated (Turner, Loftis, & Blackwell, 2006).

Solution #4: Degrading Neuronal Enzyme Modulation

For many individuals, providing the substrate alone is not effective enough. This is because neurotransmitter synthesis pathways are extremely complex. Certain enzymes are responsible for the synthetic process. These, in turn, are facilitated by still other cofactors. Mineral and vitamin depletion will often be rate-limiting steps of conversion. For example, in the case of serotonin, tryptophan must first be converted to 5-hydroxytryptophan via the enzyme tryptophan hydroxylase. 5-hydroxytryptophan, in turn, requires an enzyme called aromatic l-amino acid decarboxylase, combined with vitamins B6, B12, folate, and magnesium in order to

finally manufacture serotonin (Burns, Brett, Olverman, Nagatsu, Lee, & Williams, 1996). For this reason, supplementation of all these is often necessary to support proper synthesis until the body begins to autoregulate with more efficiency.

As another example, pyridoxal phosphate (the active form of vitamin B6) is a required cofactor for the decarboxylation reactions of aromatic L-amino acid decarboxylase (AAAD). In turn, AAAD's decarboxylation reactions facilitate the conversion of L-dopa to dopamine, as well as 5-HTP to serotonin, and tryptophan to tryptamine. Many individuals who are deficient in AAAD have single nucleotide polymorphisms and other variations of a gene that encodes this enzyme. Thus, they may require more vitamin B6 than the average person to facilitate decarboxylation reactions (Scherer, McPherson, Wasmuth, & Marsh, 1992; Lauritsen, Borglum, Betancur, Philippe, Kruse, Leboyer, & Ewald, 2002).

For patients with enzymic genetic abnormalities, the rapidly growing field of epigenetics holds much promise. This is the study of functionally relevant modifications to the genome that do not involve a change in the nucleotide sequence. Certain environmental factors have been shown to "switch on" or "switch off" genes that cause symptoms. Many environmental factors in the diet can change gene expression or cellular phenotype: food additives, food colorings, and benzoate preservatives have been shown to increase hyperactivity, depression, and anxiety. Phytic acid, lectins, caffeine, nicotine, and alcohol can also interfere with neurotransmitter synthesis dramatically in some individuals. Due to changes in the way these foods are produced and processed, some people (especially children) cannot tolerate the gluten and casein proteins found in wheat[10] and dairy. Misdigested by the gastrointestinal system, these proteins produce morphine-like compounds and other potent neurotoxins that bypass the blood-brain barrier,

[10] Researchers are currently attempting to recreate ancient perennial strains of wheat that contain less complex gluten proteins (Robins, 2007; Shwry, Tatham, Barro, Barcelo, & Lazzeri, 1995).

resulting in less than optimal brain function (Watson, Smith, Sponaugle, & Jones, 2010; Hyman, 2009).

Even those without enzymic genetic abnormalities are often still deficient in vitamin and mineral cofactors because their psychopathology hinders consistent healthy eating habits. Brown & Gerbarg (2012) explain,

> Children and adults with below-normal levels of essential vitamins—B1, B6, B12, folate, C, and D—may benefit from supplementation. People with ADHD often have suboptimal diets because they either don't have the organizational ability to shop and cook properly, or they don't have the patience to sit and eat regular meals. Moreover, their appetite may be suppressed by stimulant medications…A randomized, double-blind 3-month study of 245 children with low serum levels of vitamin B or C found that treatment with vitamin supplements reduced levels of aggression and antisocial behavior as well as improving cognitive performance compared to placebo. In 20% of the children given supplements, the mean IQ scores increased 16 points (Schoenthaler & Bier, 1999) (pp. 114-115).

Parents may consider such methods as first-line treatments because they are much safer than stimulant medications. An increasing number of studies are revealing the long-term impact of stimulant drugs. Even long after the child is off the medication, maladaptation persists in the brain:

> These structural changes include dendritic lengthening and branching, and an increase in the spine density of cells in key brain regions (nucleus accumbens and frontal cortex) associated with learning and addiction. Since these anatomic changes persist long after drug-taking has ended, researchers speculate that they may be the basis of the behavioral sensitization (craving and addiction) and/or psychotic features which emerge in some individuals during periods of extended drug abstinence. In animal studies, researchers have also found that stimulant-induced changes in neuronal architecture interfere with the acquisition of new skills or behaviors…
>
> Although stimulants have been prescribed to children in the United States for more than six decades, it appears that no one has performed an epidemiological study which has followed subjects prospectively through adulthood in order to monitor specifically for the onset of dopamine-related neurological disease. Of particular concern are the tics which arise in many children during active treatment, due to disruptions in dopamine transmission within the basal ganglia (the movement centers of the brain). If chronic stimulant

> therapy during childhood or adolescence begets changes in gene expression and neuronal connectivity within the nigrostriatal pathways, one must wonder about the potential for these drugs to contribute to Parkinson's disease or other dyskinetic disorders with advancing age (Jackson, 2005, pp. 267-268).

Because, as recently discovered, the heart has a complex nervous system of its own (Wisneski & Anderson, 2009), another concern regarding long-term use of stimulant medications is heart disease. Between the years 1990-2000, 569 children had to be hospitalized for heart conditions (186 of whom died) due to stimulants (Merlin, 2009). What is the implication, long-term, even for those not hospitalized? Jackson (2005) continues,

> Since animal studies have documented structural changes in the heart tissue following treatment with stimulant drugs (e.g. lamellar membrane accumulations within the cells of the myocardium), one must wonder about similar effects in humans. In other words, the cardiac effects of childhood medication might manifest themselves in adulthood (similar to the delayed effects of anabolic steroids) by contributing to the pathogenesis of cardiomyopathy, arrythmias, or other forms of heart disease (p. 268).

A Complementary Approach

By comparison, neurosubstrate loading, enzyme modulation, and supplementation of other necessary cofactors for neurotransmitter synthesis do not pose the same risks (Ross, 2002), nor are they mutually exclusive to the use of stimulants and other medications. Though they may take longer to effect change, holistic (also known as "functional") approaches can be combined with the use of medication in acute situations. Then, after the brain has regained its ability to autoregulate to a higher degree, the medications can be removed. Brown and Gerbarg (2012) explain,

> The relatively new field of complementary and alternative medicine (CAM) covers a wide range of biological, psychological, and mind-body treatments that can augment the benefits of prescription drugs and sometimes reduce or obviate the need for those drugs. CAM therapies should be considered in every treatment because, overall, they have fewer side effects than drugs, and many actually have additional health benefits. Concern about drug side effects is one of the major

> issues driving consumers and clinicians to explore these promising new nonpharmaceutical treatments (p. 3).

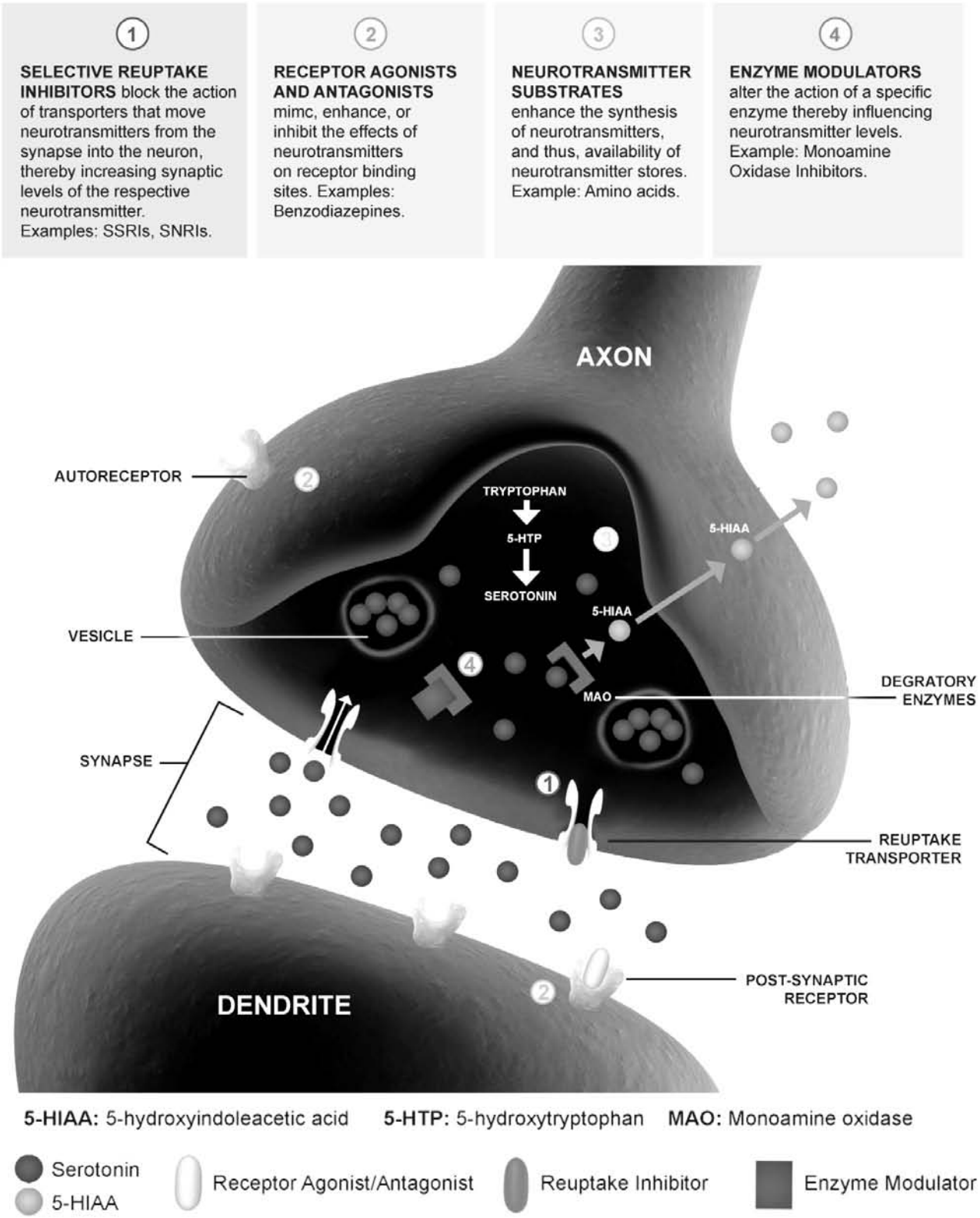
To summarize, the four primary psychopharmacological points of intervention we have covered are: reuptake inhibition, receptor modification, substrate loading, and enzyme modulation (these are illustrated in Figure 7). There are many components to the nervous system and many ways in which we can alter the brain—for better, or for worse. No doubt the years ahead will inundate us with even more new findings in neuroscience and epigenetics. But one principle seems here to stay: When prescribing solutions to problems, especially those of non-acute nature, one needs to consider how the solution will affect the system *over the course of time*.

It should also be remembered that pharmaceutical and non-pharmaceutical solutions are both to be found in the four mechanisms of action listed above. No single method or agent is inherently evil, nor a "cure-all." In fact, the line between pharmaceutical and non-pharmaceutical agents blurs with each passing year. Some of the newer non-pharmaceutical "nutraceuticals" are extremely potent, and need to be used with as much caution as pharmaceuticals (preferably under the care of a clinician trained in psychopharmacology). Lastly, pharmaceutical tapering decisions are required, in most states[11] (including Michigan), to be overseen by a physician.

Having examined the physical dimension of psychopathology now in detail, let us zoom back out and try to apply some of this information to a case study.

[11] Exceptions are Louisiana and New Mexico, where psychologists are given prescribing rights after pursuing post-doctoral certification in psychopharmacology. Several other states, including Michigan, are considering bills that would allow psychologists to taper and prescribe psychotropic medications.

Figure 7: Psychopharmacological Points of Intervention



CHAPTER 6: CASE STUDY

Meet Bob

Bob is the struggling Christian man we met earlier, who dislikes his job and is often angry toward his family. Based on his clinical intake and a neurotransmitter test, we know he has a stressful career and a problem synthesizing serotonin (both results of a fallen world). Even so, the condition is not so severe that his volition is gone. It is clear that he still has a choice when he lashes out at others (result of the flesh). Further, because of his continued anger and unforgiveness toward his wife and daughter, we have to assume the possibility of demonic attack (result of the devil). Bob experiences a certain amount of gratification and relief after he has an explosive episode. Later, however, he feels guilt and shame, knowing that what he did was hurtful. This has been going on for several years. However, he does not know how to change.

The Physical Dimension

Without further genetic testing, we do not know specifically why Bob has a problem synthesizing serotonin. However, further testing is not necessary. Though there can be many reasons why the body has reduced synthesis capacity, psychopharmacological agents will often increase synaptic levels of serotonin regardless. Because this is not an acute problem, Prozac and Zoloft are not recommended because of the risk of side effects. These SSRIs could potentially cause vomiting, nausea, insomnia, and diarrhea in the short-term and sexual dysfunction and weight gain in the long-term (Hirschfeld, 2003), not to mention long-term decline in CNS autoregulation and protracted allostatic load. Instead, substrate loading with tryptophan and 5-HTP, as well as cofactors like pyridoxal phosphate (the active form of vitamin B6) for enhancing decarboxylation reactions, is indicated.

Further, there may be other neurotransmitter imbalances. If the test shows excesses in his glutamatergic system, it may be necessary to avoid processed foods that contain glutamate. The

FDA allows glutamate to be marketed under 30 different innocent names such as “natural flavorings” and “hydrolyzed protein.” For some people, these agents can produce inflammation in the body and the brain (Franco, et al., 2007; Pacheco et al., 2007). This interferes with the glutamate decarboxylase enzyme, elevating excitatory glutamate levels (McElligott & Winter, 2009). Therefore, dietary changes may be recommended if serotonin support by itself does not produce desired changes.

Environmental factors, like glutamate, can certainly be a contributing factor to intermittent explosive disorder. But so can unforgiveness. Sophisticated neuropsychological experiments show that memories actually change the way the brain works. Wisneski and Anderson (2005) describe the first of these experiments, and the birth of a new field of research called *psychoneuroimmunology*:

> In the past two decades, biomedical research has changed our understanding of body systems. It is now known that there is a complex network of feedback, mediation, and modulation among the central and autonomic nervous systems, the endocrine system, the immune system, and the stress system. These systems, which were previously considered pristinely independent, in fact, interact on myriad levels. PNI [psychoneuroimmunology] is concerned with the various interactions among these body systems and provides the underpinnings of a scientific explanation for what is commonly referred to as the mind-body connection.
>
> In 1964, George Freeman Solomon wrote “Emotions, Immunity, and Disease: A Speculative Theoretical Integration.” In this paper, Solomon first used the term *psychoimmunology* and introduced the concept of a medical link between our emotions and immune systems (Solomon, 1964). In 1975, Rober Ader expanded on Solomon’s work and coined the term *psychoneuroimmunology*. During that same year, Ader and his colleagues published the startling results of their research on the conditioned immune response in a rat population (Ader and Cohen, 1975). The rats in the experimental group were injected with cyclophosphamide (an immunosuppressive agent) while simultaneously being given drinking water flavored with saccharin. The rats were later given only the saccharin flavored water, but no cyclophosphamide. To the researcher’s surprise (not to mention the rest of the medical community), the rats continued to evidence immune suppression. This was the first documented example of Pavlovian conditioning of the immune response (pp. xxvii-xxviii).

In the same way that Pavlov eventually conditioned dogs to salivate when they heard a bell ring (even though there was no food), these researchers conditioned rats to slowly die (some of them did die) when they tasted the sweetened water again in the second experiment (even though there was no poison). Extinction of the conditioned response in several of the rats did not occur until it was too late. Their immunosuppression and death was caused by a *memory*, not an extrinsic biological or chemical substance. This shows that reactivation of memories can actually alter the neuroimmunological system at a subconscious level.

What is the application of this to anger and unforgiveness? When someone holds onto these memories, they are continuing to have an effect on the brain—changing neurotransmitter and immune system levels, long after the stressor is physically present and producing its effect. Furthermore, just as the rats were allowed to return to full health in between the two experiments, sometimes individuals can go for years between stressors in perfect mental health. When stressors from long ago (e.g. childhood neglect or memories of a domineering authority figure) are reactivated later in life (now Bob has a boss at work that demeans him and treats him like his father did), these begin to impact neurology at a subconscious level. While a rat's brain is probably not capable of benefiting from cognitive therapy, a human brain can begin to be restored through cognitive interventions. By beginning to resolve Bob's previous stressors in childhood, a therapist can actually change the way his brain works.

The Emotional Dimension

Now we have begun to move into the emotional dimension of Bob's psychopathology. Therapy addressing his past stressors will certainly be helpful. However, if the therapist's "homework" for the client only includes such things as working on assertiveness skills, writing a seething letter and throwing it away, or punching a pillow, these will not address Bob's

underlying anger and unforgiveness. They are the emotional equivalent of Zoloft or Prozac. If you need to punch a pillow, go ahead and do it. But that's not going to fix your underlying problem. Many counselors do not ever get around to dealing with sin. Instead, coping mechanism after coping mechanism is applied. This is akin to continually applying patches on an inefficient system without ever addressing its underlying cause.

When sin (unforgiveness) finally is addressed, Bob may begin to present denial, rationalization, or projection. He may even cite Scripture to defend his anger: "Hate what is evil" (Rom. 12:9) and "To fear the Lord is to hate evil" (Prov. 8:13). Whether such defense mechanisms are instigated demonically or not, it is surely similar to Satan's use of Scripture in an attempt to lead Jesus into sin. A Christian therapist, when working with a client who believes in the truth of the Bible, can do as Jesus did. She can show how these Scriptures are true, but they are balanced by others on the subject. Yes, we are to hate what is evil. Yes, anger is not necessarily sinful—but it can easily lead to sin. As the ESV (a more literal translation) puts it: "*Be angry and do not sin*; do not let the sun go down on your anger" (Eph. 4:26).

Didactic methods (i.e. teaching) can be helpful for some "Type A" personalities, but Socratic approaches (i.e. questioning) probably work best for the majority of clients. A gentle therapist can help a client think about:

- With whom am I angry?
- What do I gain by remaining angry?
- Am I viewing myself the way that God would see me?
- Do others see me the same way that God sees me?
- What about myself do I wish others understood or accepted more?
- What do I like about myself, and why?

- What does God like about me, and why?
- Is there anything that could make God love me less? Are there things in my life that can grieve him?
- Without regard to how difficult it might be, what specific things do I think God wants me to change (behaviors, beliefs, attitudes, etc.)? Why?
- For each of these, why have they not changed yet?
- What is the cost of not partnering with God to make these changes?

The Spiritual Dimension

At this point we are now moving into the spiritual dimension. So far we have seen how short-term emotional and short-term physical solutions, that do not address underlying problems, can leave a person even weaker and more dependent than before. Does this principle apply equally to the spiritual dimension? It seems that it does:

> When an evil spirit comes out of a man, it goes through arid places seeking rest and does not find it. Then it says, "I will return to the house I left." When it arrives, it finds the house unoccupied, swept clean and put in order. Then it goes and takes with it seven other spirits more wicked than itself, and they go in and live there. *And the final condition of that man is worse than the first* (Matt. 12:43-45).

A man's *topos* ("place" or "opportunity for influence"; see discussion on p. 7) is likened to a house in this passage. For some reason, the evil spirit (demon) that was occupying the *topos* was forced to come out. From the context, we do not know exactly how this happened, except that there was some kind of "cleansing" used on the house. Presumably, as long as this cleansing was in effect, the demon did not want to come back. But evil spirits do not like being outside their *topos* (aka host) for long periods of time (v. 33; cf. Matt. 8:31). As soon as the "cleansing" agent was removed, the demons came back in greater numbers. Though the house had been cleansed, it was still unoccupied.

What does this short parable have to teach us today? From the context, Jesus is comparing the man's *topos* to the generation of people during his ministry on earth. He says at the end of the parable, "And the final condition of that man is worse than the first. *That is how it will be with this wicked generation*" (v. 45). Many people were receiving the spiritual blessings of Jesus' earthly ministry (their houses were being cleansed). And they were always clamoring for more miracles (v. 38). Yet Jesus let them know (very subtly, as always in his parables) that, after he left, they would be even worse off than before—because their houses would still be empty. They had experienced the blessings of cleansing, but they had not invited God's Spirit to live in them. Especially when combined with Ephesians 4:26-27 (cf. 2 Cor. 2:10-11), we know this state of affairs can take place, to some degree, in the life of a Christian. While a true Christian must have some degree of the Holy Spirit's presence in his life, some have "put out the Spirit's fire" (1 Th. 5:19). Even Christian leaders and "spiritual" people can open themselves to attack in this way. Written for an audience of pastors, Alemayehu (2011) offers these insights:

> The parable illustrates that the entrance of Jesus into someone's life not only drives out the evil power, but also purifies the person. This is not nearly enough, though. We need to comprehend the importance of remembering that the house representing the life of an individual should be cleansed but not empty.
>
> When we attend revival meetings, we tend to experience similar outcomes. Jesus drives out the evil powers in our lives, but the fire of such revival can easily go out, and we risk a worse condition. And this leads to utter discouragement, and we ask the familiar question "why?" Why does the impact of our revival meetings seem so short lived? The answer? The house stands empty. The house can be cleansed and put in order during the revival but, if the abode becomes empty afterwards, chances are it will be repossessed.
>
> And the latter condition will be worse than the former.
>
> How can this dangerous state be avoided? The simple answer is, Do not leave the house empty. Cleansed of the evil spirit, the heart is clean, but do not leave it empty—let Jesus dwell in it as a permanent occupant of the heart. The apostle Paul gives us a two-step action plan:
>
> **First, be filled with the Word.** "Let the word of Christ dwell in you richly" (Col. 3:16). This is a command—not an option. The following steps will help us make this verse a living reality.

> 1. Read and/or listen to the Word. The incarnate Word that dwelt among us must also dwell in us in the form of the inspired Word. Says the psalmist: "I have hidden your word in my heart that I might not sin against you" (Ps. 119:11). Without the Word of God and His commandments dwelling in our hearts and guiding the course of our lives, we are constantly exposed to the danger of coming under the influence of the evil one (see also Rom. 10:17; Rev. 1:3).
>
> 2. Study the Word in-depth. A deep and continual study of the Word is necessary so as to be filled with it; a superficial reading or listening will not get us very far (2 Tim. 2:15; Acts 17:11; Ps. 119:11). As Jacob wrestled with the Angel of the Lord and firmly declared that he would not leave Him until he received His blessing, we should also struggle with the Word of God until we clearly see Jesus Christ and His purpose in our lives.
>
> 3. Obey the Word. We should not focus on Bible study to satisfy our curiosity, but rather to maintain a fulfilling relationship with Jesus. "If anyone loves me," said Jesus, "he will obey my teaching. My Father will love him, and we will come to him and make our home with him" (John 14:23).
>
> **Second, "be filled with the Spirit"** (Eph. 5:18). To avoid the risk of leaving the house empty, the house should be filled with the Spirit…a Spirit-filled Christian will join Paul in saying, "I have been crucified with Christ and I no longer live, but Christ lives in me. The life I live in the body, I live by faith in the Son of God, who loved me and gave himself for me" (Gal. 2:20).
>
> Due to many strange practices ascribed to a filling with the Spirit, some are afraid of it. However, fear should not lead us to an unwise act of "throwing out the baby with the bathwater." The existence of the counterfeit experiences cannot be an excuse to forfeit the genuine gift ("The Message of the Parable" section, para. 1-10).

Alemayehu's critique of this passage, and its application for today, is spiritually mindful without being dramatic. While it is true that severe cases of demonic possession can only be resolved by prayer for deliverance and by demonic rebuke (Mark 9:25-29), the overall thrust of both the Old and the New Testament shows that living righteously is enough to keep demonic activity at bay. As Grudem (1994) points out,

> If we think of the overall emphasis of the New Testament epistles, we realize that very little space is given to discussing demonic activity in the lives of believers or methods to resist and oppose such activity. The emphasis is on telling believers not to sin but to live lives of righteousness…[he lists several passages]
>
> The preceding passages suggest, then, that where there is a pattern of persistent sin in the life of a Christian in one area or another, the primary responsibility for that sin rests with the individual Christian and his or her choices to continue that wrongful pattern (see Rom. 6, esp. vv. 12-16; also Gal. 5:16-26). Nevertheless, there could possibly be some demonic influence contributing to and

> intensifying that sinful tendency. For a Christian who has prayed and struggled for years to overcome a bad temper, for example, there might be a spirit of anger that is one factor in that continued pattern of sin (pp. 420-423).

We do not want to err on either side of this dangerous spectrum. Satan would be happy with either outcome. Either we can ignore him, denying his existence or his impact on our lives. The other extreme is always being dependent on another "spiritual breakthrough" or "spiritual deliverance," without truly letting one's life be changed by the Word of God and the Holy Spirit. Going to revivals and praying with others will certainly make an evil spirit want to leave and go "through arid places seeking rest" because it doesn't like being in the presence of God. However, once this "cleansing" event is past and the house is still "unoccupied," there is nothing preventing the evil spirit from returning. Though we do not understand why, somehow this gives an evil spirit even greater license to bring others with it. Prayers for deliverance will be a short-term solution, but a long-term solution will require dealing with the underlying sin.[12]

Bob will need to forgive his wife and daughter and repent of his anger. Otherwise, no matter how much prayer, or therapy, or medicine received, he is unlikely to improve very much. Moore (2009) concludes:

> Innumerable strongholds are connected to an unwillingness to forgive. Left untreated, unforgiveness becomes spiritual cancer…Beloved sister or brother, the bottom line is…unforgiveness makes us sick. Always spiritually. Often emotionally. And, surprisingly often, physically (p. 220).

In this chapter, we have seen the result of Bob's unforgiveness in all three areas: It affects relationships within his family, evil spirits in the spiritual realm, and his own body's nervous and immune systems. Moreover, his diagnosis is also created by a combination of serotonin

[12] Leaders in the "deliverance ministry" movement of the 1970-1990s recognized that phenomena similar to Matt. 12:43-45 was occurring in their ministry. Though still incorporating prayer for deliverance into their work, they have also realized the need for repentance of sin, and proper biblical grounding, in the life of a severely demon possessed individual (N. Manwiller, personal communication, 2012). See Albright (1997) and Logan (1995) for excellent practical theologies on the subject of severe demon possession.

deficiency, excitatory glutamate levels, and memories subconsciously triggered by his current work situation. All of these myriad interactions between components facilitate Bob's intermittent explosive episodes. Complex almost seems like an understatement.[13]

[13] Although outside our scope, the meta-analysis of a disorder is also worth considering. In this case, why is intermittent explosive disorder increasing in both adults and children? This question borders on the study of sociology, but answers would provide significant insight into how to treat the disorder. This question can be approached from a complex systems model, especially utilizing the concept of "tipping point": the point at which previously rare phenomena become rapidly and dramatically more common.

From a physical perspective, our suffering has dramatically changed. We no longer suffer from many of the physical diseases we used to. Yet, why is everything from serotonin deficiency and food intolerance to Asperger's and autism on the rise? For example, according to the CDC (2012), *1 in 88 children* now has an autism spectrum disorder. Improved diagnoses cannot fully explain this increase. From an emotional perspective, why have some sins become intolerable (e.g. slavery, discrimination, child abuse, etc.), while others are now accepted (e.g. adultery, promiscuity, homosexuality, etc.)? From a spiritual perspective, why is our culture rapidly becoming discontent with cherished scientific theories and turning to Eastern spiritual worldviews? These questions can also be addressed from a theologically integrated model utilizing the concept of "tipping points" within complex systems.

CHAPTER SEVEN: THEOLOGY OF HOLISM

Etymology

The concepts of holism, emergence, and complex systems are not really new. Interestingly, the English word "holism" has a long history and comes from the same root word as "health" and "holy." From the Greek *holos*, holism literally means that all components in a system (of any kind) are present and working to create health. To be holy means "set apart for the work of God." Yet, it is difficult to be used for God's work when a person is not whole. Indeed, as Sobel (2010) shows, if you research these words' etymology, "you will find yourself in a historical hall of mirrors that reflects linguistically linked etymons. Holism, whole…holy … [and] health are all part of an extended family stretching back to ancient Greece and Old English" (para. 2).

Even going back to ancient Hebrew, the concepts of "whole," "health," and "set apart" are linked. In its very first use in history, the word holy is used to describe the "wholeness" of creation week and the fact that it was "very good," which is why God made it "set apart." After the fall of creation, to be made "whole" again required one to be "set apart." The most "set apart" elements for God's use were, as a symbol to the Jewish people, required to be "whole" (e.g. cut stones could not be used for altars, those with defects could not serve as priests, etc.).

Though not under Old Testament ceremonial laws today, we are still commanded to care for our health because it is an aspect of our holiness (1 Cor. 6:19-20; 2 Cor. 7:1). The concepts of wholeness, holiness, and health are frequently linked as analogies in the New Testament (Rom. 11:16; Eph. 2:21; 4:13; 4:16; Col. 2:16; James 3:2,6). By the same token, "unwholeness" and "unholiness" are also linked: "[An unholy person] goes into great detail about what he has seen, and his unspiritual mind puffs him up with idle notions. He has lost connection with the Head,

from whom the whole body, supported and held together by its ligaments and sinews, grows as God causes it to grow" (Col. 2:18-19). In 1 Corinthians 12, Paul devotes an entire chapter using the human body's holistic nature as a model to teach about specialization (different gifts) within a complex system (the Body of Christ). He also illustrates a systemic problem (sexual immorality) that is causing cascading failures within the system (a church body) using an analogy of yeast and dough (1 Cor. 5:6).

Though holistic thinking may seem like the latest craze, and even though the terms used in complex systems theory are recent, the concepts they describe are anything but novel. Holism is really an ancient, and thoroughly biblical, concept.

The Concept of "Heart" in Scripture

Because the human psyche is so complex, problems are not always easy to identify and solve. In a sense, cure is not possible on this side of heaven. Perhaps this is why Jeremiah writes, "The heart [Hebrew *leb*: "mind, will, or thought"] is…beyond cure. Who can understand it?" (17:9). Likewise, Solomon says, "The purposes of a man's heart are deep waters, but a man of understanding draws them out" (Prov. 20:5). It takes great understanding even to begin to "draw out" what is truly happening in our own or another person's heart. Counsel from another can be helpful; even better are several others working in partnership. Again we read in Proverbs, "Plans fail for lack of counsel, but with many advisers they succeed" (15:22).

Even with many counselors, much understanding, and innovative technology, however, our hearts will never be completely whole until we finally reach heaven. All earthly systems, from railroad systems to nervous systems, have been corrupted. Right now, even among the healthiest of us, our thoughts could be graphed on a landscape occupying suboptimal peaks. This

landscape is formed by many elements of creation's beauty, our love for others, and the presence of God—but is now distorted by a cursed world, fleshly desires, and demonic influence.

Suffering, and even death, can be caused by the sins of others—at no fault of our own. For example, Abel's shed blood is described as righteous in Matthew 23:35. Other suffering is caused by our own sin, as was the invalid's in John 5. Jesus told him, "See, you are well again. Stop sinning or something worse may happen to you" (5:14). The etiology of some suffering, however, is neither our own sin, nor the sin of others. For example, when Jesus' disciples asked him, "Rabbi, who sinned, this man or his parents, that he was born blind?," Jesus answered, "Neither this man nor his parents sinned" (John 9:2-3). In this case, a cursed world seems to be the cause for the blind man's suffering. Many forms of suffering (e.g. stepping on a thorn) are more the result of living in a cursed world than anything else. Indeed, our own bodies groan inwardly (when not outwardly), along with the rest of creation, waiting for restoration (Rom. 8:22-23).

The point is that suffering can be *more* or *less* the consequence of one's volition. In addition, it is likely that a person's suffering is not completely her fault or entirely her "fate." Even the narcoleptic (from chapter 1) probably has some amount of control over her disorder. If, in the course of speaking with others, she becomes aware of the benefits of getting more sleep, exercising more, reducing her use of stimulants (coffee, caffeine, etc.), neurosubstrate loading, or dietary changes—yet chooses not to apply any of these interventions because they are inconvenient, it would seem that her culpability increases. As the Apostle James says, "Anyone, then, who knows the good he ought to do and doesn't do it, sins" (4:17).

At the beginning, we also considered an individual with antisocial personality disorder. Though much of his suffering is likely the result of his own volition, test results of his hormone

levels might show he has elevated testosterone and cortisone (Kuepper, et al., 2010), compromising his ability to function properly. It really is very hard to imagine a DSM disorder that is completely the result of one's own volition or completely outside of one's control. For this reason, we must view such disorders as "complex," and treat accordingly.

Certainly the prevention of suffering has to be multifaceted. This is evidenced, for example, as Paul counsels Timothy to, "Flee the evil desires of youth" (2 Tim. 2:22), gives him medical advice, "Stop drinking only water, and use a little wine because of your stomach and your frequent illnesses" (1 Tim. 5:23), and prays for him: "Night and day I constantly remember you in my prayers" (2 Tim. 1:3). Paul makes sure to cover all the bases.

Hope for Now, Cure for Beyond

By God's grace, we have the ability to mitigate suffering through counseling, medical care, and prayer. Based on the doctrine of *common* grace (Grudem, 1994, pp. 657-667), we know these measures will even have effect in the lives of unbelievers. Certainly many non-Christians are willing to heed counsel based on biblical principles even if they deny the source of its authority. Many non-Christians even brighten at the knowledge that you are praying for them (if you are allowed to say that, where you work). A clinician may choose to incorporate prayer while working on case paperwork or other clinical duties. We are probably no busier than the Apostle Paul, and he made time for it. Besides, prayer may very well be our most potent weapon when it comes to suffering that, with any degree, is demonic in origin.

In contrast to the limited resources available to an unbeliever for overcoming suffering, Christians have access to one great advantage (even though we don't always choose to use it). Mitigation of suffering is best achieved, as a believer, through the sanctifying work of the Holy Spirit. The Holy Spirit is our greatest counselor (Greek *paráklētos*: "one who consoles or

intercedes"), and can often be the greatest source of comfort when human counselors are unavailable. The Holy Spirit brings us strength and joy when facing suffering (1 Th. 1:6), because we know its purpose is for our sanctification. The Apostle Paul, who experienced everything from poor eyesight to multiple shipwrecks, says in Romans 5:3, "We also rejoice in our sufferings, because we know that suffering produces perseverance; perseverance, character; and character, *hope*."

Our final and true hope for conquering suffering lies beyond this life. Finally, in heaven, our sanctification will be complete and we will be restored to perfect wholeness, holiness, and health. There will be no more sin, no demons, and no more cursed world. Our neurotransmitters (or whatever means God chooses to regulate our new, glorified bodies) will be restored, as it was in the beginning.

Do "Talents" = Neurotransmitters?

I would like to close this chapter with a final thought—one that I admit is slightly speculative. Earlier, I cited a portion of a passage from Jeremiah. Here it is again, in extended form:

> The heart is deceitful above all things and beyond cure. Who can understand it?
> "I the LORD search the heart and examine the mind, to reward a man according to his conduct, according to what his deeds deserve" (17:9-10).

This passage seems only further brought to life by advances in brain imaging, showing vast heterogeneity of brain function and architecture. Who can understand it? We only understand more clearly, now, how much we do not understand. Moreover, it can sometimes be difficult for us to know a person's degree of capacity or culpability. While it may not always be clear to us what is going on in the heart of someone else, God knows. Even though we cannot

fully know the capacity of others, God can. On the last day, when he is the Judge, he will see into each person's heart. What will we find on the last day?

Jesus tells a parable about three men who were given talents by a master, who left them to be productive with these various sums of money:

> To one he gave five talents of money, to another two talents, and to another one talent, each according to his ability. Then he went on his journey. The man who had received the five talents went at once and put his money to work and gained five more. So also, the one with the two talents gained two more. But the man who had received the one talent went off, dug a hole in the ground and hid his master's money.
>
> After a long time the master of those servants returned and settled accounts with them. The man who had received the five talents brought the other five. "Master," he said, "you entrusted me with five talents. See, I have gained five more."
>
> His master replied, "Well done, good and faithful servant! You have been faithful with a few things; I will put you in charge of many things. Come and share your master's happiness!"
>
> The man with the two talents also came. "Master," he said, "you entrusted me with two talents; see, I have gained two more."
>
> His master replied, "Well done, good and faithful servant! You have been faithful with a few things; I will put you in charge of many things. Come and share your master's happiness!"
>
> Then the man who had received the one talent came. "Master," he said, "I knew that you are a hard man, harvesting where you have not sown and gathering where you have not scattered seed. So I was afraid and went out and hid your talent in the ground. See, here is what belongs to you" (Matt. 25:15-25).

I've always looked at this passage and thought, concerning the last servant: "Alright, you can do it! You only need one more talent!" If he finished with two, then he would be doing just as well as the other guys. The temptation for those who have been given little in this life (deficient neurotransmitters, genetic problems, brain abnormalities) is to bury what little "talent" they have and resort to special pleading. Although concerning a different topic, Harris (2000) describes it this way:

> Imagine that you're an art student in an art class. You and dozens of classmates are learning from a master painter. One day your teacher displays a painting of his own. It's an incredible work of art, and he wants each of you to copy it.

> You're about to begin working when you turn to look at the person next to you. You're surprised to note that he has a larger brush than you and a different kind of canvas. You look around at the rest of the class. Some students have acrylic paint, others watercolor, still other oil—and everyone is using different colors. Though you all have the same assignment, you each have completely different materials. This frustrates you. Some students have materials you would prefer for yourself. Why should they get them?
>
> You're not the only student to notice the disparity. A hand goes up on your left. A girl with only a ragged brush and three pale shades of blue on her palette is noticeable agitated. "This isn't fair," she tells the teacher. "How do you expect me to duplicate your painting when the people around me have so many more colors to choose from?"
>
> The teacher smiles. "Don't worry about the other students," he says. "I've carefully chosen brushes and paints for each of you. Trust me. You have what you need to complete the assignment. Remember, your goal is not to create a painting that mirrors the person next to you, but to do your best with the materials I've given you to replicate *my* painting (pp. 30-31).

God wants us to imitate his Son, Jesus. He knows that none of us is able to do this perfectly; this is why we need him. Furthermore, some of us are given better health, talents, paintbrushes, etc. to accomplish the job than others. A person struggling with mental illness (or any illness, for that matter), especially after doing everything he can to overcome his deficit, can often feel guilty or frustrated he cannot do better. But he should not give up hope! As the Lord spoke to Paul, "My grace is sufficient for you, for my power is made perfect in weakness"; because of this, Paul says, "Therefore I will boast all the more gladly about my weaknesses, so that Christ's power may rest on me…For when I am weak, then I am strong" (2 Cor. 12:9-10). God knows our weaknesses and understands them, even when others do not: "The Lord does not look at the things man looks at. Man looks at the outward appearance, but the Lord looks at the heart" (1 Sam. 16:7).

What are the implications of this for those of us who do not struggle with these things? Are we not unlike the servants who were given two, or five, talents? What if the servant given five talents, instead of investing it, were to compare himself with the servants who were only

given one or two? Let us suppose, in this thought experiment, the servant with only one has doubled his investment. Meanwhile, the servant with five talents has still not done much of anything because he is content comparing himself with the “weaker” servants.

On the last day, what will we find? Will the girl, who only had pale blue paints to work with, receive first place instead of the artist of a magnificent portrait—one who had whole rooms of painting supplies at his disposal? Will an autistic person, who honors God to the degree he knows how, be found to have accomplished more than the Bible professor? “Judge nothing before the appointed time; wait till the Lord comes. He will bring to light what is hidden in darkness and will expose the motives of men’s hearts. At that time each will receive his praise from God” (1 Cor. 4:5).

If we are fortunate enough to not struggle with these things, we can adopt Paul’s advice of, “Do not think of yourself more highly than you ought, but rather think of yourself with sober judgment, in accordance with the measure of faith God has given you” (Rom.12:3). We must remember, “From everyone who has been given much, much will be demanded; and from the one who has been entrusted with much, much more will be asked” (Luke 12:48). For those who have the privilege and responsibility of teaching others (from behind the pulpit, the stethoscope, or the notepad), we “will be judged more strictly” (Jam. 3:1).

Let us do our best in this life, with the talents we have been given, so we may hear those words on the last day: “Well done, good and faithful servant! You have been faithful with a few things; I will put you in charge of many things. Come and share your master’s happiness!” (Matt. 25:21).

CHAPTER EIGHT: ANTIREDUCTIONISM

Theoretical vs. Methodological

The material we have covered in these last several chapters was highly interdisciplinary in nature—due to the complexity of the thesis statement argued. We have addressed concepts from theology, complex systems theory, systems biology, neuroscience, and back again. Most scholarly writing is more reductionistic in its analysis and presentation. Methodological studies are the most reductionistic, focusing on the collection of empirical data and its interpretation. This method relies heavily on what is called *a posteriori* analysis (reasoning which is dependent on experience). Theoretical studies are less reductionistic, analyzing data from previous methodological studies and interpreting them largely through *a priori* analysis (reasoning which is independent of any experience, other than the experience of learning the language in which the propositions are expressed).

Both types of study—theoretical and methodological—are necessary to advancing knowledge in any field. However, there is an increasing trend in the academic sciences to promote theoretical scholarship, especially interdisciplinary theoretical submissions. With exponentially increasing data within specialties, it is sometimes difficult to see how all the pieces fit together. These birthing pains led to the development of complex systems theory, or "complexity science," an attempt to further understand complex phenomena.

However, someone might ask, "Is this theoretical form of study capable of producing understanding on par with methodological study? Especially regarding the spiritual dimension, do we really know all this stuff about heaven and demons and the biblical account of redemption is true—or is it just speculation?" These are fair questions. After all, such theoretical study often will not directly analyze components within a system empirically.

In short, my answer is this: Theoretical study is often lacking, compared to methodological study, because conclusions drawn can be based on faulty presuppositions. Methodological study, if conducted properly according to the scientific method, will always be based on valid presuppositions. However, having said this, theoretical study has the *capacity* to outrank methodological study both in terms of scope and strength.

Concerning scope, I want to explain why methodological study is sometimes incapable of producing solutions to complex problems (especially related to psychopathology). This discussion will be the most complex we have undertaken, because it concerns the validity of complex systems theory itself. Wikipedia (2012) introduces this topic succinctly,

> Although "breaking complex phenomena into parts is a key method in science," (Lane, 2009) there are those complex phenomena (e.g. in psychology, sociology, ecology) where some resistance to or rebellion against this approach arises, primarily due to the perceived shortcomings of the reductionist approach. When such situations arise, some people search for ideas that supply "an effective antidote against reductionism, scientism [belief that science is the only way to discovering truth], and psychiatric hubris" (Radden, 2004). This in essence forms the philosophical basis for antireductionism. Such rebellions against reductionism also implicitly carry some critique of the scientific method itself, which engenders suspicion among scientists that antireductionism must inherently be flawed.
>
> Antireductionism often arises in academic fields such as history, economics, anthropology, medicine, and biology as dissatisfaction with attempts to explain complex phenomena through being reduced to simplistic, ill-fitting models, which do not provide much insight about the matter in hand.
>
> An example in psychology is the "ontology of events to provide an anti-reductionist answer to the mind/matter debate…the impossibility of intertranslating the two idioms by means of psychophysical laws blocks any analytically reductive relation between…the mental and the physical" (Davidson, 2001) (para. 1-3).

Many forms of antireductionism do not view the scientific method as the "end-all, be-all" way of arriving at truth. For this reason, as the article above indicated, antireductionism is often viewed with suspicion by other scientists because they think it must be inherently flawed. But it is not flawed, and here's why:

The Scientific Method

The scientific method—a method of inquiry that analyzes observable, measurable, and repeatable evidence—cannot, itself, be validated by the scientific method. The definition of "validated" is important here. If, by validity, we mean that the scientific method does what it claims to do—that is, adds to the body of analyzed empirical evidence on a given topic—then the scientific method *is* valid. To prove this, we could simply amass a representative, random sample of methodological studies, formulate the criteria for success (values for correlation, goodness of fit, X-square, p-value, etc.), and then determine the statistical significance of the "success" cases relative to the sample and the control group(s).

However, if, by validity, we mean the scientific method is capable of grounding itself, we have to conclude it cannot. Any attempt to prove otherwise results in a circular argument (e.g., "Bob used the scientific method to prove the scientific method"). In fact, the scientific method is not something that is even capable of being evaluated empirically, because it is not physical in nature—it is a "method." This is the same problem that reductionistic theories of knowledge face, such as empiricism (also called positivism). This theory of knowledge is self-refuting because it cannot validate (ground) itself. It sates that all "justified beliefs" must be reducible to claims about observable phenomena. However, theories are not observable. Therefore, according to the theory itself, we should not believe it to be true. Slife and Williams (1995) explain further,

> Scientific method was formulated by philosophers, the preeminent dealers in ideas. These philosophers, *not* scientists, are responsible for the package of ideas now called *scientific method*. Scientists may *use* science, but they are often unaware of the ideas formulated by philosophers that lie hidden in their scientific methods…
>
> This lack of awareness is partly because scientific method cannot itself be experimentally tested. Method has what some philosophers call a bootstrap problem. Just as those who wear old-fashioned boots cannot raise themselves into their air by pulling on the straps of the boots, so practitioners of the scientific method cannot use its methods to validate it. Some people argue that the many

> successes of science demonstrate its validity. However, this argument contains the same bootstrap problem. Citing *success* begs the question (pp. 4-5).[14]

Having looked at the similarity between empiricism and the scientific method, we can now draw their distinction. In contrast to empiricism, the scientific method *is* validated (of the grounded variety)—but not in itself. It is validated by a combination of propositions, which can further be validated by even more basic propositions. Some of the most basic propositions (or presuppositions) that ground the scientific method are listed here, which I will call the "4 Ls syllogism."

The 4 Ls Syllogism

1. Legal: Laws of logic exist, both semantically and ontologically (actuality of being).
2. Lasting: These laws will continue to operate tomorrow as they do today.
3. Learning: We have the ability to learn these laws, remember them, apply them to empirical (observable) evidence, and teach these applications to others.
4. Liability: We have a moral obligation to study and present these laws, and their applications to empirical evidence, truthfully.
5. Therefore, we can, and should, study empirical evidence rigorously (aka "the scientific method").

Let us review the 4 Ls syllogism again, seeing how the scientific method fails to validate these propositions in itself:

1. Legal: The laws of logic, "Modus ponens," "modus tollens," "disjunctive syllogism," and dozens of others, are not physical entities. They cannot be seen, measured, touched, smelled, etc. Similarly, irreducible mathematical axioms such as Zermelo-Frankel axioms for set theory, Peano axioms for number theory, and Euclidean

[14] This is also known as "Hume's problem of induction."

axioms for geometry are completely abstract. Unlike traffic laws, these laws do not have anything *physical* grounding them.

2. Lasting: How do we know these laws haven't changed during the course of a certain experiment? If the laws of logic were revised, amended, and updated like other laws from time to time, our ability to conduct science would be impossible. A common response is, "Laws of logic have always stayed the same in the past; therefore, they will stay the same in the future." However, this is a circular argument. It is the exact same thing as saying, "In the past, the future has been like the past; therefore, in the future, the future will be like the past." The word "therefore" in both sentences is implying that the future will be like the past. But this is the very thing to be proved. Whenever we use past experience as the argument for why something will happen in the future, we are presupposing number 2.
3. Learning: Concerning our ability to learn these laws, and even the veracity of our observations about the physical world, the scientific method is not available for comment. Our physical senses could be severely compromised; perhaps we are trapped within a "matrix." Science fiction aside, Haldane put it more practically: "If my mental processes are determined wholly by the motions of the atoms in my brain, I have no reason to suppose that my beliefs are true…and hence I have no reason for supposing my brain to be composed of atoms" (see p. 1).
4. Liability: Even if laws of logic do ontologically exist, and even if these laws remain the same over time, and even if we do have the ability to perceive reality accurately, why *ought* I to present my scientific findings truthfully? This seems to imply a moral obligation.

If these four propositions cannot be validated by the scientific method, what can ground them? Secular philosophers of science debate this question increasingly, and have found no satisfying answers. As Christians, we understand these propositions are grounded in an unchanging, perfectly good Lawgiver, who has created us in his image (aka "God"). Moreover, the 4 Ls can also be used to validate Scripture.[15] These conclusions must come by faith (i.e. certainty without sense experience). This type of faith is not irrational; indeed, it is the only worldview that makes thinking rational. For this reason, theology is sometimes called the "queen of the sciences" (Howard, 2006). The point is that, whereas the scientific method cannot ground the 4 Ls, God himself can:

1. Legal: Laws of logic are grounded in God himself: "In the beginning was the Word [Greek *logos*: "ontology" or "logic"], and the Word was with God, and the Word was God" (John 1:1).
2. Lasting: "Dominion and awe belong to God; he establishes order in the heights of heaven" (Job 25:2). Though God will occasionally violate the physical manifestation of this order to demonstrate his glory for a specific purpose, he usually maintains this order, "sustaining all things by his powerful word" (Heb. 1:3).
3. Learning: Because God himself is orderly, we should be orderly in our thoughts and actions (1 Cor. 14:32-33). Though "we see but a poor reflection as in a mirror," we still have the ability to gain partial knowledge during this life (1 Cor. 13:11-12). In fact, gaining knowledge is an honor: "It is the glory of God to conceal a matter; to search out a matter is the glory of kings" (Prov. 25:2).

[15] Refer to footnote on p. 2.

4. Liability: The Apostle James would also warn researchers, "Who is wise and understanding among you? Let him show it by his good life, by deeds done in the humility that comes from wisdom. But if you harbor bitter envy and selfish ambition in your hearts, do not boast about it *or deny the truth*. Such 'wisdom' does not come down from heaven but is earthly, unspiritual, of the devil. For where you have envy and selfish ambition, there you find disorder and every evil practice. But the wisdom that comes from heaven is first of all pure; then peace-loving, considerate, submissive, full of mercy and good fruit, *impartial and sincere*" (James 3:13-17).[16]

Application to Antireductionism

As we have seen, the scientific method is based on even more foundational principles. Thus, an approach to analyzing and interpreting data that uses foundational principles (logic, math, our ability to learn and remember, etc.) will be capable of producing knowledge, quite apart from any empirical evidence or *a posteriori* reasoning.

For example, if I wanted to write a theoretical paper on the statement, "the tangent to a circle intersects the radius of that circle at right angles," or "the square root of two cannot be

[16] This line of reasoning, which I have called the "4 Ls syllogism," is adapted from the *transcendental* argument for the existence of God. A careful reader might ask, "If the scientific method is grounded in more basic principles, and if these basic principles are grounded in God, what is God grounded in?" The answer, simply put, is that God grounds himself. This is what the scientific method was unable to do. Again, the definition of "valid" is extremely important here. Technically, a circular argument is not invalid. For example, "Bob is at work right now. The time is 9:00 a.m. Therefore, Bob is at work" contains a conclusion that was validly reasoned from one of the premises. Similarly, "Bob uses the scientific method at work to conduct rigorous experiments; therefore, his findings are accurate" is also subtly circular, for the reasons listed above. Both sentences are completely valid (and sound, given the premises are true). Yet, we typically don't use these arguments because they don't add to our knowledge. However, once you have reached your ultimate presupposition, you cannot gain any more knowledge. This ultimate presupposition must be able to validate (ground) itself and every other proposition. As Lisle (2009) puts it,

"There are two things to remember about circular reasoning when it comes to an ultimate commitment. 1) It is absolutely unavoidable. 2) It is not *necessarily* fallacious. First, some degree of circular reasoning is unavoidable when proving an ultimate standard…an ultimate standard cannot be proved from anything else, otherwise it wouldn't be *ultimate*…Second, not all circles are fallacious. Remember that begging the question is not actually invalid, but it is normally considered a fallacy because it is arbitrary…An ultimate standard must do more than simply prove itself. It must provide a basis for proving absolutely everything that is knowable…Non-Christian circles [of reasoning; e.g., empiricism] turn out to be self-refuting, rather than self-attesting, and they cannot account for the preconditions of intelligibility…So the question is *not* "Which worldview uses some degree of circular reasoning?" They all do. The question is, "Which worldview is actually able to do this *successfully*?" (pp. 145-147).

expressed as the ratio of two integers," I could prove these statements without using empirical evidence or *a posteriori* reasoning. Similarly, I can have knowledge (i.e., a justified, true belief) that George Washington existed and was the first president of the United States, though I cannot reproduce him, and I have never met him. In this case, I am relying on L1 and L3 to account for my knowledge of this fact.

Most knowledge is based on a combination of *a posteriori* and *a priori* analysis. The thesis statement of this present work is grounded, for me, in empirical evidence—both through personal experience (*a posteriori* analysis), and in the ability to analyze the experiences of others (using *a priori* analysis). However, some things I have argued cannot be proven through analyzing empirical evidence. Though the chapters on systems biology and neuroscience referred to physical entities, the statements made regarding the emotional and spiritual dimensions are incapable of comment by the scientific method. We can often test the empirical *effects* of these, but we cannot directly test the emotional and spiritual dimensions themselves. Consequently, there are at least three reasons why it is legitimate to adopt an "antireductionist" method to analyzing and interpreting data using complex systems theory (or any theoretical model grounded in foundational principles):

1) Reductionistic approaches (e.g. the scientific method) are themselves theoretical models grounded in foundational principles; 2) Some problems are so complex that they are *infeasible* to solve through methodological study. This stance is sometimes called *metaphysical antireductionism*.[17] 3) Some problems are *impossible* to solve through methodological study,

[17] Most researchers (who have studied these matters) hold at least to metaphysical, if not ontological, antireductionism, which is the reason for increasing interdisciplinary theoretical scholarship. Such scholarship is capable of producing knowledge with as much, or greater, strength and validity as the scientific method. Strength is evaluated using model theory (a form of mathematical logic that examines semantic statements by means of using syntactical elements of a corresponding language). Validity (of the grounded variety) can be shown using inter-theoretic indispensability arguments. The scientific method, itself, relies on inter-theoretic indispensability arguments. Marcus (2010) explains, concerning science's relationship to mathematics,

because the system's components are non-physical. This is sometimes called *ontological antireductionism*. Non-empiricists (including evangelical Christians) hold to ontological antireductionism (Rosenberg, & Kaplan, 2005). It should be understood that "antireductionism," used in this sense, does not imply that reductionism is evil or bad. It simply means that reductionistic methods (e.g., the scientific method and methodological study) are not capable of solving complex problems or (on an ontological view) interpreting *all* data.

A Firm Foundation

Though theoretical study is capable of producing knowledge on par with methodological study, it can easily be flawed if based on faulty presuppositions. This is why it is necessary to examine the underlying presuppositions of theories before using them to interpret data. Slife and Williams (1995) capture this sentiment well,

> Behavioral scientists, by definition, study and explain a broad range of human behaviors. However, if you ask a half dozen behavioral scientists how they would explain a friend's rude behavior, you would likely get a half dozen *differing* replies. As the behavioral scientists consult the theories and models of their disciplines, they would offer explanations ranging from "she's been conditioned by her environment" to "her more selfish id has overcome her more civilized ego" to "she freely and willfully acted rudely toward you."
>
> Explanations from the behavioral sciences can be so numerous that it is easy to get confused or frustrated. You might want to ask, "Just what is the *right* explanation anyway?" Most behavioral scientists would undoubtedly sympathize. Some would respond to your frustration by encouraging you to "tolerate the ambiguity" of behavioral science, because it reflects the ambiguity of life. These behavioral scientists have given up trying to discern the most correct theory or

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"The indispensability argument in the philosophy of mathematics, in its most general form, consists of two premises. The major premise states that we should believe that mathematical objects exist if we need them in our best scientific theory. The minor premise claims that we do in fact require mathematical objects in our scientific theory. The argument concludes that we should believe in the abstract objects of mathematics…Indispensability arguments need not be restricted to the philosophy of mathematics. Considered more generally, an indispensability argument is an inference to the best explanation which transfers evidence for one set of claims to another. If the transfer crosses disciplinary lines, we can call the argument an inter-theoretic indispensability argument. If evidence is transferred within a theory, we can call the argument an intra-theoretic indispensability argument" (intro., para. 3; sec. 8, para. 1).

For this reason, we can use the principles of mathematics to study physics; physics to study chemistry; chemistry to study biology; biology to study (the physical dimension of) psychology; psychology to study sociology, etc. I have made the case that the lowest level of inter-theoretic indispensability argument is knowledge of God himself, because he is necessary to ground foundational principles (including mathematics).

> explanation. Other behavioral scientists, however, consider it part of their job to separate the theoretical wheat from the chaff and differentiate the bad from the good explanations. Many theories, they would say, can be eliminated, because they do not measure up to certain standards. Other theories can be tested to see whether they hold up under the scrutiny of science or practice.
>
> The problem is that these standards and this scrutiny do not typically expose the *implicit ideas* of the theories. All theories have implied understandings about the world that are crucial to their formulation and use. Even if we accept multiple explanations as the "way it is" in the behavioral sciences, this acceptance provides no mean of recognizing the assumptions "hidden" in these multiple explanations…
>
> For example, the explanation you adopt for your friend's rude behavior will affect the way you respond to her. Hidden in any of the differing explanations you can adopt is an assumption about determinism. Did forces out of your friend's control, such as conditioning from her environment or chemicals in her brain, *determine* her actions? If your answer is yes, you might feel sorry for her and want to console her. After all, she could not help herself. If, however, you decide that she could have responded in a more polite manner—that is, her rudeness was *not* determined—you might be angry with her and wish to confront or avoid her…
>
> It may be a very long time before behavioral scientists come up with a single theory that explains everything, if indeed this is ever possible. In the meantime, laypersons and professional people alike must adopt in their daily lives explanations and theories that have hidden costs and consequences…
>
> The difficulty is that in the behavioral sciences, relatively little attention is paid to assumptions and implications. Students are often taught the various theories for understanding behavioral science phenomena, but rarely is this teaching enriched by directly examining the assumptions and implications hidden within these theories. Criticisms of the theories are sometimes offered, but these criticisms seldom do more than scratch the surface.

This present thesis was an attempt to do more than scratch the surface. We have looked at the very foundations, examining our model's presuppositions in this last chapter. I agree with Slife and Williams it is unlikely, in this life, that we will come up with a single theory that explains everything. In fact, I know this will not be the case: "Now we see but a poor reflection as in a mirror; then we shall see face to face. *Now I know in part*; then I shall know fully, even as I am fully known" (1 Cor. 13:12).

The mirror we use to examine data will never be perfect. Nevertheless, I think we can wipe the mirror down, turn on some more lights, and look into it as closely as we can.

CONCLUSION

The Effects of Postmodernism

Slife and William's book, *What's Behind the Research?*, quoted on the previous page, is an example of postmodern skepticism. This movement seeks to analyze the underlying presuppositions (often called "biases" or "assumptions") of any model or theory. Originally coined in 1949, "postmodernism" referred primarily to the rethinking of values within the arts, society, and culture as a whole. More recently the term is being used to refer to a rethinking of how research and science should be conducted. Postmodernism is changing the face of psychology, the practice of medicine, and how we understand spirituality. In short, postmodernism is changing the way we think. Whereas the scientific method gave us modernism , now postmodernism seeks to liberate itself from the scientific method. This movement led to the philosophical "science wars" of the 1990s (Ashman, & Baringer, 2001), and is partially responsible for a return to a holistic paradigm. Complex systems theory and interdisciplinary theoretical scholarship is the result of dissatisfaction with the strictures of methodological study. As a generation that believed in "scientism" gives way to a new generation that is increasingly antireductionist, we are also seeing a marked rise in pluralistic spirituality.

Obviously this movement is not without error; postmodern skepticism often finds itself in philosophical trouble. The most noticeable problem becomes evident when postmodernism tries to deny truth itself. Although Slife and Williams believe in God and hold to absolute truth, many postmodern authors do not. When such authors argue, vigorously, that laws of logic are only semantic and not absolutely true, they expect us to believe their arguments absolutely—not just semantically. But this is a self-refuting proposition; the claim "nothing is really true" cannot, according to itself, be really true. According to such authors, we are free to create our own

meaning from a written text because it is fundamentally impossible to understand authorial intent. Yet, this stance refutes itself; for if it is true that we cannot understand authorial intent we would not be able to understand the postmodern author to begin with. Similarly, when pluralism adamantly claims that exclusivist religions (e.g. Christianity) are too narrow, this claim itself turns out to be exclusivist. A "pluralistic" view, interestingly, cannot accept all views. There is just no getting around the fact that some things are true and some things are not.

For all of postmodernism's pitfalls, however, this movement *is* correct to analyze underlying presuppositions. We *should* be skeptical of a theory that says all knowledge must come through empirical observation. As we saw in the final chapter, such a theory does not stand the test of scrutiny. However, postmodern researchers are understandably at a bit of a loss. Now that we are using model theory to ground interdisciplinary theoretical research,[18] what will ground model theory?

Christian researchers can contribute to interdisciplinary theoretical work with a firm understanding of why this is even possible. As ones who believe, "all truth is God's truth," we can see how everything fits together and is grounded in God himself. We have no reason to be afraid of postmodernism or of examining our most basic beliefs. Though written primarily for how the church should respond to postmodernism, these words of advice apply to our topic as well,

> As I see it, postmodernism provides an unprecedented opportunity for self-examination. By its very nature, postmodernism offers us a chance to think long and hard about why we do the things we do. It forces us to wrestle with our beliefs and our traditions, our programs and our theology, all in an effort to uncover those aspects of our faith that are really and truly God's—and, by extension, those that are not.
>
> Still, the concept of deconstruction is a scary one. We get nervous at the thought of deconstructing anything—primarily because we're afraid if we pull our religion apart, we may end up with nothing in the end. We picture home repair

[18] Refer to footnote on p. 71.

> projects gone wrong—with heaven or hell hanging in the balance. Never mind an angry spouse. What if we aren't able to fit the pieces back together in any kind of coherent whole? What then?
>
> I guess that's why I prefer to use the words "unwrap" or "unpackage." As Christians responding to the challenge of postmodernism, we're not attacking our faith, we're simply unpackaging it. We're daring to pull off the shells of sentiment and tradition in confidence of finding a pearl of great price inside…Whereas postmodern secularists may deconstruct everything down to its essence, postmodern Christians ultimately will retain at least one absolute, Jesus Christ (p. 27).

This thesis was an attempt to deconstruct or "unpackage" psychopathology down to its core and reconstruct a coherent model using only the presuppositions of Scripture and complex systems theory. I purposely avoided the basing of any argument on previous psychological theory. My purpose in this study was to build, from the ground up, a model for the diagnosis and treatment of psychopathology that would be theologically integrative and capable of incorporating interdisciplinary data.

I hope and pray some may find it useful in their work.

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Appendix: *History of the Development of Complexity Science*