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Bad Brains: Crime and Drug Abuse from a Neurocriminological Perspective

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Abstract Research into the biosocial correlates of antisocial behavior has revealed the importance of integrating sociological findings with evidence flowing from genetics and neuroscience. The present study represents a step toward such integration by offering an in-depth overview of neurocriminology, which is the study of the brain and how it affects antisocial behavior. We consider the role of the brain in both antisocial/criminal behavior as well as in drug use/abuse. We highlight various regions/systems in the brain that have been identified as targets for intervention and as areas in need of more study. This knowledge equips us with the foundation to think translationally about how to promote mental health, adaptive behavior, and well-being among drug using criminal offenders.

Keywords Neurocriminology · Cognitive neuroscience · Drug · Criminal behavior

As a discipline, criminology has traditionally drawn on social factors to explain the etiology of antisocial behavior. Yet, over the past few decades a growing body of evidence has shown that biology is also important to consider when studying antisocial outcomes (Barnes et al., 2014; Caspi et al., 2002; Raine, 1993; Miles & Carey, 1997;

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Rhee & Waldman, 2002; Moffitt, 2005). Referred to broadly as *biosocial criminology*, this area of study considers the impact of genetics, biology, neuroscience, and social influences on antisocial behavior and crime. These relationships are inherently complex. Crime is a social construct, and the occurrence of criminal behavior is necessarily tied to the laws and mores of a society. Drug use (and misuse) provides a good example for how these strata intersect.

Illicit drug abuse is a crime, and it is strongly influenced by both biological and social factors (NIDA, 2014; Volkow & Fowler, 2000). It is also strongly correlated with other forms of antisocial behavior (Karberg & James, 2005). As we will see, some instances of drug abuse and other forms of crime have common underlying biological influences. Recognizing the influence of biology on drug abuse and crime is really about understanding how biology influences individual differences in behavior. Neuroscience has become a crucial nexus for understanding these relationships as research increasingly clarifies how biology and the environment change brain function, and how brain function then influences our behavior.

Criminologists, practitioners, and policy makers can benefit from understanding these relationships better and incorporating them into their work. Unfortunately, many are unfamiliar with the basics of neuroanatomy and the important insights that neuroscience research has to offer. Additionally, much of the primary literature in neuroscience assumes the reader has a firm handle on the concepts and language of the discipline. The criminological discipline would benefit from an overview of some basic principles of neuroscience and how they relate to practical issues in criminology. This is what we intend here. We begin by discussing the structure and basic functional properties of the brain. We provide an overview of brain-imaging techniques and describe their value for contemporary neuroscience research and criminology.

We describe how drugs affect the brain and we then consider how some contemporary models of addiction are informed by neuroscience and genetics. Finally, we examine how these same principles can be applied more generally to facilitate an understanding of the roots of antisocial behavior.

Brain Structure and Function

The brain is our central processing unit. It controls everything we do both voluntarily and involuntarily (e.g., walking, breathing, digesting). It processes the information we collect through our senses and arranges that information in meaningful ways. This includes forming memories and associations, eliciting emotions and motivation, and initiating or inhibiting our actions. Discovering how the brain "works" has been one of the most important scientific endeavors of the last century. Although it had long been known that the brain houses mental processes related to vision, hearing, and executive functioning like rational thought (Descartes, 1972[1664]), only recently have we begun to understand the fundamental mechanics of these processes. Though an in-depth coverage of brain functioning is beyond the scope of this paper, a working knowledge of a few basics can aid our understanding of how neuroscience can help us understand criminal behavior. Readers interested in examining these topics in more depth are encouraged to seek out any number of excellent resources (e.g. Kolb & Wishaw,

2014; Clark, Boutros, & Mendez, 2010), which we have relied on for much of these summaries.

Neurons are the cells that make up the nervous system: the brain, the spinal cord, and the peripheral nerves throughout the body. They are the organic matter that (largely) makes up the brain's structure (i.e., the gray matter). Neurons are uniquely specialized to communicate with each other via electrical/chemical signals (Hodgkin & Huxley, 1939). There are approximately 100 billion neurons in the human body and over 100 trillion (10^{14}) connections between them.

Interestingly, neurons do not physically connect together like roads on a highway. Instead, two adjacent neurons come together at a synapse—a small gap—and must send chemical messages (neurotransmitters) across the space of the synapse. A cartoon image of the synapse formed by two neurons is provided in Fig. 1. In general, a single neuron consists of a cell body, dendrites, and an axon. The cell body houses the cell nucleus and most of the familiar machinery of a typical cell. It is depicted as the large green portion of the *post*-synaptic neuron on the right of Fig. 1. The receptive extensions, called dendrites, receive the chemical messages from the axons of *pre*-synaptic neurons, depicted in Fig. 1 as the slender portion of the neuron that is covered by pink sheaths. These sheaths are what make up white matter in the brain (also called myelin), which insulates the conduction of electrical signals down the entire length of the axon. A single cell body receives messages from many axons, and the combined effect of these messages determines whether or not that cell will carry a signal downstream to the next neuron. If the neuron does propagate the signal, this electrical current is relayed down the axon and is called an action potential.

An action potential is an all-or-none electrical current that travels the distance of an axon relatively quickly (due to the insulating myelin). The chemical portion of the electrochemical signal takes place at the axon terminal; the end of an axon, near the synapse. Once the electrical signal reaches the end of the neuron, tiny vesicles holding chemical messengers known as neurotransmitters release their contents into the synaptic cleft that separates the two neurons from one another. Neurotransmitters carry the message—now in chemical form—across the synapse to the post-synaptic neuron and this sequence of events is repeated again in that neuron. Neurotransmitters add a level of complexity to the information that can be communicated between neurons. There are

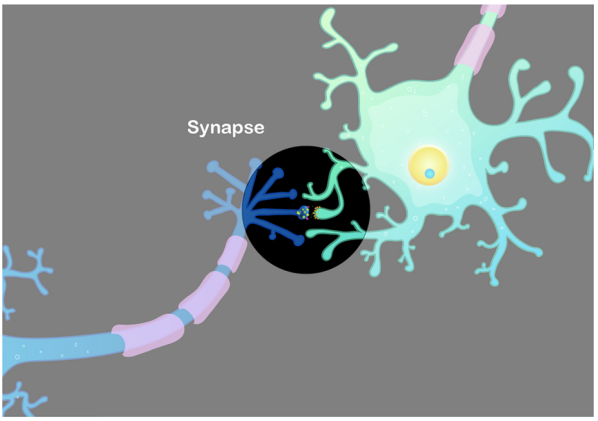

Fig. 1 Diagram of a neuron. Source: https://images.nimh.nih.gov/public_il/image_details.cfm?id=669

dozens of different neurotransmitters, each with their own specialized functions. For example, a single neuron may receive an excitatory signal (*fire an action potential*) from the neurotransmitters released by one neuron, while simultaneously receiving an inhibitory signal (*don't fire*) from the neurotransmitters released from a different pre-synaptic neuron. Only the total combined effect of many inputs will ultimately determine whether or not the post-synaptic neuron propogates an action potential to the terminal of the neuron receiving these messages.

This process is constantly occurring in each of our 100 billion neurons. Luckily, we rarely need to consider the actions of single neurons in determining behavior. This process is carried out collectively by groups of neurons with shared functions every time your brain interprets an image of the environment around you, when you hear a sound, when you decide to stand up, and when you actually do stand up. As you can imagine, there are a seemingly infinite number of messages being sent at any time in the human brain, making it extremely difficult to separate the signal (i.e., the particular electrochemical signal of interest) from the noise (i.e., all the other electrochemical signaling that is taking place) for any specific task or thought. Nonetheless, neuroscientists have identified networks of neurons that are dedicated to specific functions, as well as the roles of many neurotransmitters in this complex orchestra that plays out during information processing. Individual differences in how we think, move, perceive, remember, and behave all can be related to variation in the functions of these complex groups of neurons. Understanding these differences requires some understanding of basic anatomy and functional networks in the brain.

Structure of the Brain

Figure 2 shows the basic structure of the brain, including the cerebrum, cerebellum, and brainstem, as well as a few major interior features of the brain. At the very bottom of the brain is the brainstem, which connects the cerebrum to the spinal cord through a small hole at the base of the skull called the foramen magnum. The cerebrum and the brainstem are connected through structures in the midbrain, including a structure called the thalamus, which acts like a hub for directing sensory information coming in and messages going out. Several nuclei (small bundles of cooperating neurons) in the brainstem are instrumental in regulating basic life-support functions in the body such as respiration, circulation, cardiac function, and sleep-wake cycles. The brainstem is also the main thoroughfare for sensory information coming in from the rest of the body and motor control messages sent down the spine to the muscles.

The cerebellum is located behind the brain stem and below the rear portion of the cerebrum. The cerebellum is small and accounts only for about 10 % of the brain's overall size, yet it has a higher concentration of neurons than many other parts of the brain (Andersen, Korbo, & Pakkenberg, 1992). The cerebellum is mostly involved with the integration of motor functioning including balance, coordination, movement of the limbs, and eye movement. It is also involved in coordinating some higher cognitive functions (i.e., learning and memory) by acting as a relay between other parts of the brain (Roskies, Fiez, Balota, Raichle, & Petersen, 2001); however, its precise role in these higher cognitive functions is not well-understood, and still subject to intense investigation. Our focus in this paper will primarily involve well-understood functional networks in the cerebrum and midbrain.

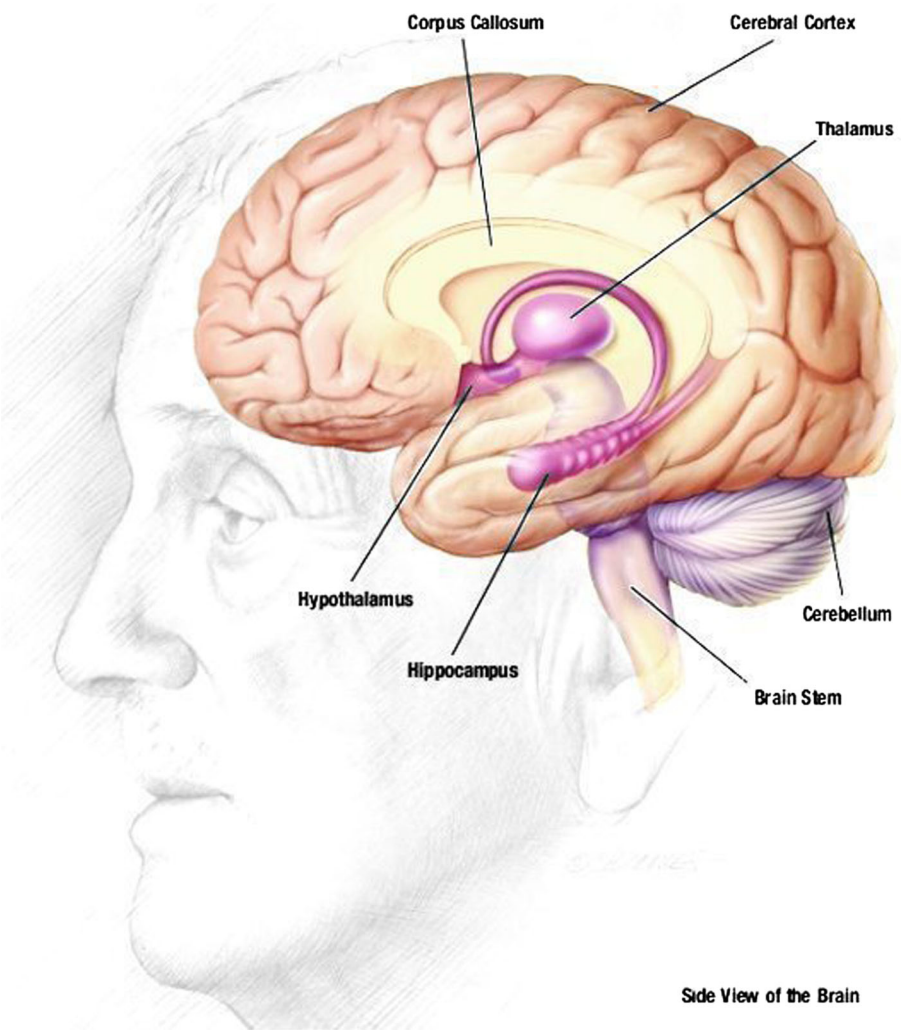

Fig. 2 Diagram of the human brain. Source:http://www.wpclipart.com/medical/anatomy/brain/human_brain_drawing.jpg.html

The cerebrum makes up the vast majority of the brain's mass. It is separated into two hemispheres (left and right), connected by the corpus callosum located in the upper interior of the cerebrum (see Fig. 2). The outer surface of the cerebrum (the cerebral cortex) is further divided into four lobes (frontal, parietal, temporal, and occipital), demarcating basic landmarks for relative anatomical positions (see Fig. 3). These divisions are more like topographical references than true indicators of function. To be sure, brain functions are rarely confined to one location. Rather, modern neuroscience research has clearly revealed the interdependence of various brain regions for even the simplest functions (Koch, 2012). Nonetheless, it is important to note the major lobes of the brain for essential anatomical references when discussing functional networks.

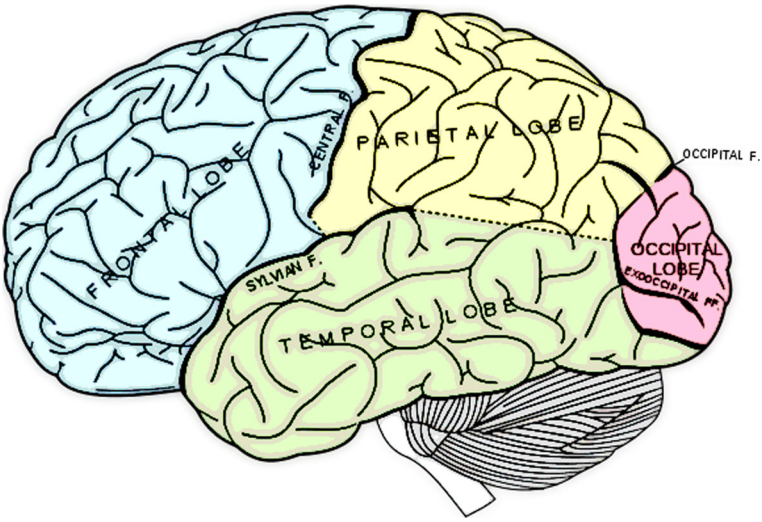

Fig. 3 Diagram of the human brain. Source: http://www.wpclipart.com/medical/anatomy/brain/four_lobes_of_the_cerebral_cortex.jpg

The occipital lobe is located posteriorly, at the very rear of the cerebral cortex. This region is known for housing the visual system. This is where information from the eyes (light translated into neural signals) travels, in order to be synthesized and interpreted. The occipital lobe is also involved in short-term (sensory) memory where it retains trace, transient neural signals representing what someone sees. It is also involved in visual attention – directing our awareness of important features in our visual environment by amplifying these neural signals. Injuries to the occipital lobe can lead to visual impairments, hallucinations, or blindness.

The temporal lobe, located along the lower-middle sides of the cerebral cortex (just above the ears), is prominently responsible for processing auditory information but is also essential for higher order (more complex) forms of visual processing; such as recognizing familiar faces. It is also essential for forming new, long-term memories. The hippocampus (featured in Fig. 2), is located in the medial (inner) portions of the temporal lobe, and consolidates neural signals from our senses into stored representations of events. A famous patient known as H.M. had his hippocampus removed to control epileptic seizures in the 1950s. While his pre-existing memory of prior events remained intact, he could no longer form new memories. For example, he would greet people as if they were meeting for the first time, even if they had met daily since the surgery (see Milner, 1972; Squire, 2009 for more information). Injuries to the temporal lobe can cause hearing and auditory perception problems, difficulty recognizing objects and faces, generalized memory problems, or a host of other complex cognitive deficits.

The parietal lobe is located toward the top-middle portion of the cerebral cortex (near the crown of the skull) and extends anteriorly connecting with the frontal lobe. The parietal cortex includes the somatosensory cortex, which is responsible for receiving and interpreting tactile information from our entire body. Other functions of the parietal lobe include attention, complex visual processing and memory, like locating objects in space and mentally rotating three-dimensional shapes. It is also involved in

sensory integration, like combining visual information and goal-oriented movement into coordinated actions.

Finally, the frontal lobe is located in the anterior portion of the cerebrum, right behind the forehead extending back to the parietal lobe. It is the largest lobe in the human brain and its size relative to the rest of the brain is a uniquely human feature. The frontal lobe houses the essential mechanisms for initiation of all voluntary movement, including speech production. The anterior-most portions of the frontal lobe (called the prefrontal cortex, close to the forehead) are responsible for many of our most advanced human cognitive abilities. These include abstract thought, the ability to predict, plan, and control our behavior based on complex priorities, and the ability to cognitively manipulate our own emotional responses. Due to the wide range of functions managed by the frontal lobe, damage to this part of the brain can disrupt a host of cognitive functions ranging from language and attention to behavioral control. There are, in fact, startling cases of frontal lobe injuries leading to impulsive and aggressive behavior (Brower & Price, 2001; Raine, 2013), substance abuse (McKinlay, Corrigan, Horwood, & Fergusson, 2014), and even acting on inappropriate sexual urges (Briken, Habermann, Berner, & Hill, 2005; Burns & Swerdlow, 2003).

Having discussed the four lobes of the cerebral cortex, it is important to also identify several key structures that are below the cortical surface. These inner parts of the brain are phylogenetically older structures that participate in many of our most essential survival functions, which have been evolutionarily preserved across species. These include systems for governing our basic drives for obtaining food and sex, recognizing reward and threat, coordinating motivated movements to pursue or avoid things in our environment, and relaying information back and forth between the cortex and the rest of the body.

The outer cortex interfaces with these subcortical structures through a network referred to as the *limbic system*. This name comes from the Latin *limbus* meaning border (limit), since these structures define the physical and functional boundaries between the cortex and subcortical systems. This network is supremely important for our understanding of how variation in brain function relates to criminal behavior and addiction. The role of the limbic system is to integrate basic emotional processes, like fear, into higher order cognitive function, like planning ahead (Maclean, 1955; Papez, 1995[1937]). This network prominently connects the amygdala, hippocampus, septal nuclei, and striatum (all subcortical structures important for motivation, emotion, and memory) to the cingulate cortex and prefrontal cortex (responsible for planning, abstract thought, and behavioral inhibition). Phylogenetically, we share these structures with all mammals (MacLean (1955) called this the paleomammalian brain), but the human cortex is more complex and capable of far more sophisticated manipulations of information.

Among these limbic structures, the amygdala is prominently involved in threat detection and anxiety, the striatum is important for reinforcement (e.g. reward and pleasure), and the cingulate cortex is important for monitoring ongoing behavior and adapting to conflicting information. The prefrontal cortex is capable of combining this information to plan and execute complex behavior. All of these neural circuits process information from our environment continually. Furthermore, they physically and functionally change as the result of experience (Kolb & Whishaw, 1998). They work together to determine our own personalized system of motivation and avoidance, which

has strong implications for both substance abuse and antisocial behavior. Recent technological advancements provide us with the ability to measure these processes in the living human brain, and these tools have been instrumental in our current understanding of how these brain systems contribute to individual differences in behavior and personality.

Assessing the Structure and Functioning of the Brain

In order to understand the role of the brain in criminal behavior and drug use, it is important to be somewhat familiar with the methods used to assess brain structure and function. Among the oldest methods for studying brain function is to carefully account for cognitive and behavioral consequences of localized brain damage. This may result from tumors, degenerative disease, head injuries, or surgeries intended to remove brain tissue responsible for epilepsy. However unfortunate, occurrences of focal lesions have been a valuable source of information about localized brain function for centuries. This method, along with studying brain tissue post-mortem, remains indispensable to cognitive science, even in modern research. Fortunately, however, improving technology has allowed the development of methods for examining the structure and function of brain tissue in living organisms.

Computer axial tomography (also known as a CAT or CT scan) was among the first methods developed for visualizing brain structure without surgery. It was developed in the 1970s and still remains in use today. During a CT scan, the brain (or any other part of the body) is X-rayed over 150 times at different angles, and a computer compiles these into a three-dimensional image from multiple slices. Denser neural regions tend to absorb more X-rays and, therefore, show up lighter as compared to less dense neural regions. This produces an image that displays internal structures, useful for revealing large-scale injuries or tissue damage. It is problematic, however, translating these low-resolution images into quantifiable measures for comparing structure across participants.

More recent technology allows three-dimensional imaging of the brain with much higher resolution using magnetic resonance imaging (MRI). MRI uses a combination of radio waves and magnetic fields to differentiate between tissues and structures in the brain. Small particles (protons) in the brain are first organized coherently by introducing a strong magnetic field. Radio waves are then transmitted through the brain causing the protons to jiggle, then realign with the magnetic field. Particles in different tissues (e.g. gray matter, white matter, cerebrospinal fluid, bone) realign with the magnetic field at different rates. These differences can be measured by receivers that detect tiny voltages created by the changes, and they are subsequently translated into high-quality images by computers.

An advantage of MRI technology is that it is extremely flexible. The magnetic fields and radio-pulse sequences can be manipulated in order to highlight different features in the tissue being imaged. For instance, diffusion tensor imaging (DTI) is an adaptation of MRI that highlights white matter tracts (long bundles of insulated neurons) in the brain. Another adaptation called functional MRI (fMRI) is able to highlight neural activity in the brain. This is accomplished by exploiting the different magnetic properties of oxygenated blood and deoxygenated blood in the microvasculature of the brain

that supply active neurons. As neurons work harder (fire action potentials more rapidly), they require more oxygen. Thus fMRI is an indirect, but highly sensitive measure of brain activity with can be localized with precision on the order of millimeters.

Several other methods are available for measuring functional activity in the brain. Techniques known as positron emission tomography (PET) and single photon emission computerized tomography (SPECT) both measure the concentration of radioactive tracers that are injected into the blood and accumulate in areas where these chemicals bind. Tracers can be designed to bind to specific sites in order to quantify things like specific varieties of neurotransmitter receptors. Otherwise, glucose molecules can be labeled and the subsequent accumulations signify local neural activity in much the same way as fMRI. This method therefore also relies on blood flow to quantify neural activity.

The only non-invasive technique available for measuring neural activity directly in the human brain is the electroencephalogram (EEG), which is also among the oldest techniques for measuring brain activity (developed in the 1920s). EEG measures electrical activity that propagates to the scalp from underlying neural activity. These signals cannot provide detailed three-dimensional maps of neural activity like some other methods. They can, however, be sampled thousands of times per second, endowing this method with superb precision for measuring the timing of specific neural events as well as cognitive information that is encoded in the frequency of neural firing.

Each neural imaging technique has its own limitations and advantages. Knowing the basic capabilities and differences between these methods is enough to provide a necessary foundation for reading and interpreting some valuable neuroscience research. Even these basics will allow for a better general understanding of how these methods are used to inform us about the relationships between brain structure, functional activity, and corresponding differences in behavior. Examining the biological underpinnings of drug abuse and addiction now will provide a meaningful context for applying this information in an immediately practical way. We will then extend these same principles to understand maladaptive and antisocial behavior more generally.

The Brain and Drug Use, Drug Abuse, and Drug Addiction

Drug use is prevalent among criminal offenders—both in and out or prison (Karberg & James, 2005). Illicit drug use can lead to incarceration as the primary offense. It can also motivate additional criminal activity, either as a means of supporting an expensive drug habit or due to the direct behavioral effects of the drugs themselves. Here we provide a primer on how drugs affect the brain and subsequent behavior. Again, a full review of psychopharmacology is beyond the scope of this article, but the essentials provided here can be well supplemented by many excellent textbooks (e.g. Stahl, 2013), which we have relied on heavily.

Psychoactive drugs are chemicals that have an effect on brain function. They exert their effects by mimicking the action of natural neurotransmitters on chemical receptors that have specific functions in the brain and other organs. As discussed above, different

classes of neurotransmitters play specific roles in the brain, and there are dozens of neurotransmitters. Even further, every neurotransmitter may bind to a variety of receptor subtypes that ultimately exert different influences on neural transmission. For instance the neurotransmitter dopamine can bind to approximately five major sub-types of dopamine receptor, each promoting different actions in various locations of the brain. Thus, psychoactive drugs exert their incredibly diverse effects by binding preferentially to neural receptors that carry out specified functional roles in perception, arousal, mood, cognition, and general physiology.

Some drugs have assorted, simultaneous effects because they bind easily to a wide range of receptors in the brain and body. Nicotine, for example, binds easily to a rather generic variety of acetylcholine receptor that is widely prevalent in the brain and other organs. It has stimulating effects in the brain, increasing cognitive arousal, but it also stimulates peripheral systems like digestion and the release of adrenaline (epinephrine). Alternatively, some drugs bind very selectively to very specific receptor types and thus they exhibit more specific effects.

The popular drug sildenafil (trade name *Viagra*), was originally developed with the intention of treating hypertension as it was designed to bind to receptors that relax blood vessels. In testing, it was discovered to bind rather more selectively to a sub-class of receptors responsible for regulating blood flow in the genitals, thus having the unexpected side-effect for which it is now heavily marketed (Katzenstein & Grossman, 2001). In short, the effect of any drug is the result of it impinging on a physical system that already exists to perform an important function in the body. Psychoactive drugs are effective at changing mood, perception, physiology, motivation, and behavior by capitalizing on the physical systems in the brain which otherwise determine these things naturally.

Psychoactive drugs that are commonly abused and carry high potential for addiction all have something fundamentally in common. They bind to receptors that influence a specific neural circuit in the brain that is responsible for reinforcing and promoting most of our motivated behavior (DiChiara & Imperato, 1988). This circuit, commonly referred to as the "reward circuit" or "pleasure center," comprises a small bundle of sub-cortical neurons originating in the midbrain and terminating at a site called the *nucleus accumbens* in the ventral striatum. This circuit is activated any time our brain determines that some stimulus in our environment is important, pleasurable, or otherwise worth remembering. Naturally rewarding stimuli like sex and food are perceived as pleasurable because they trigger a cascade of neural activity that causes a transient release of the neurotransmitter dopamine on the nucleus accumbens. Drugs that are commonly abused directly impinge on this system and flood this neural circuit with excess amounts of dopamine, up to ten times greater than what is achieved by natural reinforcers (DiChiara & Imperato, 1988). Cognitively and perceptually, the consequences of this are extremely reinforcing—that is, we are biologically motivated to attain that reward again and again.

Pharmacologically, there are several differences between the many drugs that exploit this circuit. Cocaine and amphetamines are closely related because of their direct effects on these dopamine neurons. Cocaine blockades receptors that are responsible for removing dopamine from these synapses, effectively exaggerating and prolonging these pleasurable neural signals. Amphetamines on the other hand directly increase the release of dopamine (along with several other neurotransmitters such as serotonin

and norepinephrine). As such, cocaine and amphetamines have very similar effects on this neurotransmitter system, and they share a pharmacological classification of *dopaminergic* drugs, meaning they mimic or increase the effects of dopamine.

All other commonly abused drugs including opiates, alcohol, nicotine, and cannabis, increase dopamine activity in this reward system albeit by other various mechanisms. Of course most drugs have other widespread effects elsewhere in the brain, which depend on the precise neurotransmitter system affected. In the case of drugs like alcohol and nicotine, the euphoric reinforcement attributable to the dopaminergic reward system is a relatively mild (compared to cocaine) and indirect consequence of a complex cascade of neurotransmitters. But this is paired with the primary, desired effects of these drugs on other sites of action. Alcohol, for example, reduces anxiety and has a relaxing effect due to its action on widespread receptors that blunt neuro-synaptic transmission. Nicotine may be especially satisfying after a meal due to its stimulating action in the digestive system. These primary actions influence the likelihood to use these drugs in addition to their action on the reward circuit, which reinforces their perceived value. These combined pharmacological effects are significant enough to change our patterns of motivated behavior (e.g. Vastola, Douglas, Varlinskaya, & Spear, 2002).

All else being equal, the level of euphoria achieved by a drug depends on the rapidity and potency of the dopamine release induced in the nucleus accumbens (Drevets et al., 2001). For example, opium derivatives as a general class of drug all bind to opioid receptors that are prevalent in the midbrain and spinal cord, as well as the nucleus accumbens. Opioid receptors are the same sites where our body's own endorphins and enkephalins bind, producing natural analgesic effects. Heroin is a synthetic derivative of opium that has high lipid solubility, allowing it to cross the blood-brain barrier very quickly. Heroin floods the reward circuit directly and quickly, subsequently producing potent euphoric effects in addition to the analgesic effects common to opioids. Methadone is another synthetic opioid that is commonly used to combat the withdrawal symptoms of opiate dependence. It binds to the same receptors as heroin, morphine, and other common opiates; however, it has lower abuse potential because of its relatively slow course of action, reducing the euphoric effects of the drug. Ideally the user is weaned off of the drug completely; however, methadone still carries some risk for abuse.

The physiological effects of drug abuse have lasting effects on the brain, beyond the direct action of a single dose. Over time, affected physiological systems begin to compensate for receptors that are increasingly occupied by chemicals mimicking neurotransmitters. These physical changes in cells translate to physical consequences and aversive withdrawal symptoms, which further motivate repetitive use of the drug. Moreover, the reward system adapts to high levels of dopamine, and competing (natural) rewards become proportionally less salient. It is not simply that certain drugs feel really good. Drugs that impact the reward circuit directly co-opt a neural system that has evolved, quite effectively, to manage competing rewards and motivate healthy, adaptive behavior. For some, the ability to tap into this system, at will, can trigger a cycle of behavior that naturally rewarding stimuli cannot effectively compete against (Kalivas & Volkow, 2014). Paired with the aversive consequences of withdrawal, this can be a very difficult cycle to break.

Pharmacological Treatment

Understanding the physiological mechanisms underlying reward and withdrawal has provided us with several pharmacological aids for treatment of substance dependence (O'Brien, 1997). These can be particularly effective when combined with cognitive-behavioral therapy, such that treatment addresses the user's medical, psychiatric, and social needs (NIDA, 2014). One strategy of pharmacotherapy is the initial replacement of the harmful drug with a less-harmful alternative that alleviates some of the physiological symptoms of withdrawal. A drug serving this purpose is commonly a less-potent *agonist* of the same neurotransmitter system, meaning it binds to the same sites as the drug of choice and has similar effects.

Nicotine gums, lozenges, and patches are common examples that provide users with the nicotine they are addicted to without the tar, toxins, and carcinogens found in cigarette smoke. These replacements are also less rewarding than smoking due to the slower delivery of nicotine through the skin or mucous membranes compared to the very fast delivery of nicotine by inhalation to the lungs. Over time, the dose of nicotine is ideally lessened until, hopefully, the user no longer craves nicotine. This method has been found to be moderately effective in getting smokers to quit smoking (Hughes, Golstein, Hurt, & Shiffman, 1999).

Methadone, described briefly above, is an opioid agonist commonly used to combat withdrawal from heroin. This allows addicts to be functional in society and reduces some dangerous physical and behavioral effects of dependency (Gahlinger, 2001). An alternative to methadone is buprenorphine, which is a partial agonist for opioids. Buprenorphine use has even lower potential for addiction and overdose than methadone (Vastag, 2003).

Antagonists are the opposite of agonists, meaning they bind to a receptor site but only block the site from being occupied by the drug or neurotransmitter. Naltrexone is a long-acting, orally administered opioid antagonist. This substance blocks the physiological effects of heroin and other opiates, so it reduces the pleasurable effects of the drug. It does not address symptoms of withdrawal, however. As such, naltrexone is often used in combination with an opioid agonist that helps manage withdrawal symptoms (Abadinsky, 2004). Disulfiram has been used to treat alcoholism by inhibiting the body's ability to metabolize alcohol (Mosher & Akins, 2014). This method makes the user sick (e.g., nausea and vomiting) if they drink after taking disulfiram. Acamprosate is also an alcohol antagonist that depresses receptor activation, which reduces symptoms of withdrawal in alcoholics (Lingford-Hughes, Welsh, Peters, & Nutt, 2012).

Although there are no commonly prescribed antagonists for cocaine and marijuana addiction, pharmacotherapy treatments are being researched and developed. Dopamine antagonists are available and have been tested to treat cocaine dependency, yet a number of undesired side effects preclude their use (McCance, 1997). Similarly, marijuana antagonists have been shown to decrease cravings for marijuana but the potential negative side effects tend to outweigh the benefits (Wilson, Varvel, Martin, & Lichtman, 2006).

Pharmacological interventions are a positive step in treatment of addiction, and clearly they improve outcomes for some, but they cannot cure the root of addiction. At the same time, one must recognize that the vast majority of individuals who have used

addictive drugs do not become dependent or addicted (Abadinsky, 2004; Kandel, Chen, Warner, Kessler, & Grant, 1997). As we will examine now, pre-existing individual differences in genetics and physiology can play a potent role in the likelihood that drug exposure will lead to abuse and addiction, just as one's environment and social influences can impact these things.

Vulnerability to Addiction

When considering the contribution of biology to drug use and criminal behavior, it is difficult to ignore the topic of genetics. Heritability studies have determined with remarkable consistency that substance abuse and dependence have significant genetic influence accounting for approximately 50 % of the variance in these outcomes (e.g., Barnes et al., 2014; Kendler, Karkowski, Neale, & Prescott, 2000; Kendler, Aggen, Tambs, & Reichborn-Kjennerud, 2006; Tsuang et al., 1996; Tsuang, Bar, Harley, & Lyons, 2001; van den Bree, Johnson, Neale, & Pickens, 1998; Zickler, 1999). To those unfamiliar with this variety of research, these estimates are easily misunderstood and misinterpreted (for a thorough and accessible explanation of heritability and risk see Urbanoski & Kelly, 2012). For our purposes here, it is enough to know that these estimates are derived by examining the incidence of these traits among large numbers of individuals who share quantifiable portions of their genetic variation (e.g. family members, siblings, identical twins), and further estimating the contribution of shared and unique environmental influences. Saying that addiction (or substance abuse) is half genetic does not suggest that scientists have necessarily identified the specific genetic variants involved in risk for addiction (though many have been identified; see Bierut, 2011). These estimates also cannot give us any information about the relative contribution of genetics or environmental influences in any one individual. Rather, these estimates mean that, at a population level, approximately half of variation of that trait can be accounted for by genetic inheritance as opposed to social/environmental influences (Barnes et al., 2014).

If we are comfortable with the fact that substance abuse and addiction are influenced, in part by genetic vulnerability and in part by one's environment, the next step is to recognize that genetics can never directly determine a complex behavior like drug use. This is true simply because genes do not code for behavior; they code for the expression and arrangements of proteins in the body. Genes lead to variations in brain structure and physiology (Thompson et al., 2001), which, in turn, biases behavior in predictable ways (e.g. Hicks, Iacono, & McGue, 2012). Furthermore, it should be clear that genes are not the only influence that determines brain structure and physiology. Every environmental influence that changes our behavior shapes our physiology in some way (Kolb & Whishaw, 1998). Reward, punishment, learning, discipline, social interaction, and stress all change the brain (e.g. Hackman, Farah, & Meaney, 2010). In short, the brain is the great mediator of human action, bridging genetic and environmental influences on complex behavior. This is why neuroscience is such an important level of analysis for examining variation in human behavior.

A common refrain in neuroscience is that no brain structure operates in isolation. There are many divergent and simultaneous influences on our behavior at any given moment. The learned value of rewards competes with learned expectations of

punishment. Two opposing rewards may require mutually exclusive solutions. Systems of attention in the brain bias our perception and awareness of what is relevant to consider in navigating these decisions (for an almost unbelievable example of this, see Simons & Chabris, 1999; Drew, Võ, & Wolfe, 2013). All of these processes are governed by multiple, complex systems in the brain, and variation in part of any one of these systems can influence decision-making and motivation. As might be expected, then, there are many plausible neurobiological models of addiction supported by empirical, biological evidence (for a thorough review, see Koob & Simon, 2009). Here we discuss two prominent examples among these. As we will see, these models can be further generalized to understand variation in antisocial behavior as well.

It has been suggested that some instances of substance dependence may result from a physiological vulnerability commonly referred to as *reward deficiency syndrome* (Blum, Cull, Braverman, & Comings, 1996). This model suggests that an innate limitation in sensitivity to natural rewards promotes behavior aimed at increasing dopamine levels in the brain's reward circuitry, making some individuals physically and psychologically more sensitive to the effects of drugs that pharmacologically enhance dopaminergic activity. Support for this model includes evidence of low baseline functioning of dopamine (D2) receptor function in striatal brain areas among addicts (Fehr et al., 2008; Martinez et al., 2004). This evidence is paired with molecular genetics studies that have shown a higher prevalence of several genetic variants that limit dopamine receptor function among those who are addicted to drugs and alcohol (Bowirrat & Oscar-Berman, 2005; Comings & Blum, 2000). Early support for reward deficiency syndrome focused heavily on a single genetic variant; however, more recent emerging evidence suggests many genetic variants can contribute to this pathophysiology. Drug use may temporarily ameliorate chronically low dopamine, but repeated long-term use may exacerbate the initial problem through cellular adaptations. Repeated drug exposure further decreases dopamine's efficacy (Volkow et al., 1999; Volkow, Fowler, & Wang, 2004), promoting a kind of vicious cycle.

Genetics and exposure to drugs are not the only things that impact this system. Social status can also play a role in determining these physiological vulnerabilities. This has been demonstrated by experimentally manipulating the social environments of nonhuman primates. Much like humans, other primates arrange themselves into social strata. Monkeys who find themselves in low-dominance social conditions exhibit reductions in dopamine (D2) receptors, as a consequence, and subsequently demonstrate increased reliance on available cocaine reinforcement (Grant et al., 1998; Morgan et al., 2002). Changes in their social environment were measurably changing their physiology, and this directly promoted drug use. Studies like these underscore the importance of biology and physiology as a level of analysis even when considering sociological variables.

A second prominent neurobiological model of addiction focuses on brain areas related to decision-making and the evaluation of competing rewards. Several parts of the prefrontal cortex, including the anterior cingulate cortex (ACC) are involved in these kinds of decisions. Dysfunction in these brain regions can impair mechanisms of self-control and promote substance use disorders (see Bechara, 2005; Volkow & Fowler, 2000; Kalivas & Volkow, 2014 for reviews). Specifically, the ventromedial portion of the prefrontal cortex (located just above and behind the eyes) is closely connected with the nucleus accumbens (of the reward circuit), and it is essential for

cognitive evaluations of reward and motivation. People who are addicted to drugs show hyperactivity in this brain region during craving and anticipation of drugs (Brody et al., 2002; Volkow et al., 1991). However, during periods of withdrawal and extended abstinence, substance abusers show markedly reduced brain function here compared to controls (Volkow et al., 1999, 2004). This pattern of change can be thought of as drug-induced reward deficiency as opposed to an inherent, genetic deficit; although, a combination of pre-existing deficits may also accompany a vulnerability of these brain systems to drug-induced changes. These changes in cognitive evaluation of reward are accompanied by deficits in cognitive control circuits, including portions of the anterior cingulate cortex (Goldstein & Volkow, 2002). Indeed, reduced functional activity in the anterior cingulate has been reported as a useful predictor of abstainers who are most likely to relapse (Marhe & Franken, 2014). These cognitive control circuits involving the prefrontal and cingulate cortex have also been implicated in general impairments in decision-making on standardized cognitive tests among those with substance use disorders (Bechara, 2005; Garavan & Stout, 2005).

Considering these findings together, we can begin to see how abnormalities in systems governing motivation, cognitive control, and decision-making may contribute to more fundamental vulnerabilities that occasionally manifest as substance use disorders, but may also manifest as other forms of maladaptive, disadvantageous behavior. Indeed, the model for reward deficiency syndrome has more recently been generalized to explain impulsive and antisocial behaviors as common outcomes alongside substance abuse (Blum et al., 2000). A more generalized incarnation of models emphasizing decision-making and behavioral dysregulation in addiction refers to *externalizing vulnerability* (Hicks et al., 2012). This model describes a set of highly heritable (≈.80) traits including disinhibition, antisocial behavior, impulsivity, aggression, and sensation-seeking as reliable manifestations of this vulnerability prior to the onset of substance use, but which remain highly predictive of later addiction. Considered alongside these high heritability estimates it should not be surprising that many of the same genetic variants that have been identified as contributors to addiction have also been implicated in antisocial behavior (Kreek, Nielsen, Butelman, & LaForge, 2005).

Criminal Behavior

As we stated near the outset of this paper, understanding the influence of biology on crime and drug abuse is really about understanding how biology influences individual differences in behavior. We have described some of the biological contributions to drug abuse and addiction, emphasizing the roles of the reward circuit, prefrontal cortex, and anterior cingulate cortex in models of addiction. But it should also be clear by now that many of these same diatheses are associated, more generally, with behavioral traits such as sensation-seeking, impulsivity, and disinhibition, which can promote criminal behavior as well. In parallel with the discussion above, we will now examine the contribution of several different brain areas to criminal behavior, ultimately promoting the thesis that there are multiple pathophysiological routes to criminal behavior, just as there are with substance abuse.

Medical scientists have been interested in how brain variability (and biology more generally) contributes to criminal behavior for centuries. Perhaps the most famous case

study in neuropsychology is that of Phineas Gage, a 19th century railroad worker who survived a major brain injury caused by a 3-ft steel tamping iron passing straight through his prefrontal cortex due to an unexpected explosion. Though he survived the accident, his behavior reportedly changed dramatically, making him impulsive, aggressive, and irresponsible (see Harlow, 1993[1868] for the original account). The critical part of his brain that was damaged was the ventromedial prefrontal cortex (Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). This is part of the brain that we discussed above for its critical role in models of substance abuse, as it integrates reinforcement values into higher-order decision-making.

Recent historical scrutiny suggests that this famous example is surrounded by as much legend as fact (Macmillan, 1999). Still, many more contemporary and well-documented case studies corroborate these same consequences of acute damage to the prefrontal cortex (e.g. Cato, Delis, Abildskov, & Bigler, 2004; Meyers, Berman, Scheibel, & Hayman, 1992). This is especially true when damage to this part of the brain occurs early in life (Anderson, Damasio, Tranel, & Damasio, 2000; Taber-Thomas et al., 2014). One's self-regulatory capacity is perhaps *the* strongest correlate of criminal and drug using behavior (Gottfredson & Hirschi, 1990), and neuroscience has helped to extend this conceptualization to the executive functions of the prefrontal cortex (Beaver, Wright, & DeLisi, 2007).

Recent investigations using modern neuroimaging tools have aided in this consensus as well. Cognitive neuroscientists who have specifically studied criminal offenders consistently find relationships between antisocial behavior and the structure and function of the prefrontal cortex (see Raine, 2013; Yang & Raine, 2009 for reviews). Gray matter in prefrontal regions is significantly reduced among incarcerated violent offenders compared to non-incarcerated individuals (Laakso et al., 2002; Gregory et al., 2012). Severely antisocial offenders who meet criteria for psychopathy show reduced prefrontal gray matter compared to non-psychopathic inmates (Ermer, Cope, Nyalakanti, Calhoun, & Kiehl, 2012; Gregory et al., 2012). Reduced prefrontal gray matter has also been found among non-incarcerated antisocial individuals (Raine, Lencz, Bihrle, LaCasse, & Colletti, 2000; Yang et al., 2005).

Functional imaging studies examining neural activity further corroborate the importance of the prefrontal cortex in accounting for antisocial behavior. These studies can add clarity to the actual cognitive processes that may contribute to crime. For example, Raine et al. (1994) examined the brains of murderers compared to non-incarcerated, healthy controls using PET imaging and reported reduced metabolic activity in the prefrontal cortex during a simple attention task, despite performance being equal for both groups. This might suggest baseline metabolic differences in these regions. Rubia et al. (2009) used fMRI during a similar task in order to differentiate between participants with attention deficits and antisocial behavior. Antisocial behavior was found to specifically involve ventromedial prefrontal impairments during the processing of rewards during the task.

The prefrontal cortex is not the only structure in the brain that can influence the likelihood of criminal behavior. Remember that the amygdala is a small structure in the limbic circuit that is prominently involved in processing potential threats in our environment, generally contributing to very basic emotional processes. The amygdala features prominently in neurobiological models of crime and antisocial behavior, and its role in these outcomes is multifaceted (see DeLisi, Umphress, & Vaughn, 2009 for

general review). It may be surprising that both an overactive amygdala and an underactive amygdala can promote criminal behavior in completely separate ways.

The amygdala is involved in our basic detection of threatening stimuli, governing a larger circuit in charge of the familiar *fight-or-flight* response. Direct electrical stimulation of this circuit will produce a stereotypical defensive rage response in mammals (Gregg & Siegel, 2001). People with intermittent explosive disorder (prone to easily-provoked aggressive outbursts) have been shown to have hyperactive amygdalae and poor prefrontal cortex functioning (Coccaro, McCloskey, Fitzgerald, & Phan, 2007). One convincing neurobiological model of aggressive-antisocial behavior suggests a gene by environment interaction linked to the neurotransmitter serotonin (Buckholtz & Meyer-Lindenberg, 2008). When combined with stressful rearing environments, this genetic variant promotes structural abnormalities in limbic circuitry and hyperactive amygdala activity in response to threat. This variation in physiology, in turn, makes one more prone to impulsive-violent behavior.

Likewise, physiological changes due to organic brain disease can have severe behavioral consequences. For example, Charles Whitman killed 14 people on the campus of University of Texas in Austin in 1966. Before his 90 min shooting spree, he wrote a letter stating that he had not been feeling like himself and he had been having aggressive impulses. Upon his death, his brain was examined and doctors found a tumor that was pressing against his amygdala.

Conversely, complete destruction or removal of the amygdala can produce an odd combination of docility and fearlessness in animals and humans. Sometimes described as Klüver-Bucy syndrome, these effects can make even wild animals appear tame and remain calm even in the presence of predators. It essentially makes them insensitive to threat and harm rather than easily-provoked. This kind of damage also promotes a number of inappropriate social and sexual behaviors (Klüver & Bucy, 1997; Feinstein, Adolphs, Damasio, & Tranel, 2011). The amygdala is so intimately tied with aggressive behavior that in rare cases of intractable, severe aggression in humans, surgical removal of the amygdala has been carried out as a last resort (Lee et al., 1998). Destruction of the amygdala in adults does not often lead to notable antisocial behavior; however, a poorly functioning amygdala can have dire developmental consequences if one is affected at an early age.

Psychopathy is a developmental disorder associated with severe antisocial behavior that is promoted by generally poor amygdala functioning along with other abnormalities in the entire limbic circuit (see Anderson & Kiehl, 2012; Kiehl, 2006). Children with a variety of conduct disorder paired with callous-unemotional traits (a kind of prodromal stage of adult psychopathy) exhibit poor amygdala functioning from an early age (Marsh et al., 2008). In addition to its role in fear and anxiety, the amygdala is responsible for learning from punishment and recognizing the emotional states of others (LeDoux, 2003). Developmental models of psychopathy suggest that poor amygdala functioning contributes to a unique disruption of social learning, which produce patterns of mostly self-centered motivation that is also devoid of anticipation for punishment (Blair, 2006). Psychopaths act impulsively, without anxiety, and without empathy. They do not feel regret about violating the rights of others and generally fail to reflect on these consequences of their behavior (see also Hare, 1999; Babiak & Hare, 2006). Their unique pathophysiology, however, has some distinguishing impact on their specific presentation of criminal behavior. Psychopaths, for instance, are less

likely to act out in emotional-reactive displays of violence, but are more likely to commit predatory, instrumental violence (Anderson & Kiehl, 2014; Cornell et al., 1996).

The examples provided here are not intended to be an exhaustive account of neural contributions to crime. Rather, they are intended to demonstrate that multiple, divergent physiological mechanisms in the brain have the capacity to promote criminal behavior. This parallels the multifaceted mechanisms that support one's likelihood to abuse drugs or become dependent on them. Furthermore, it should be clear that some of these mechanisms overlap to promote more generic vulnerabilities that can simultaneously promote the highly correlated behaviors of drug abuse and antisocial traits together. Finally, espousing the view that biological variables influence drug abuse, addiction, and criminal behavior is certainly not meant to suggest that these outcomes are invariably predetermined and immutable. Just the opposite is true, in fact. Understanding how these physiological systems work is the first step in understanding how these systems are ultimately amenable to change. This knowledge equips us with the foundation to think translationally about how to promote mental health, adaptive behavior, and well-being among criminal offenders.

Summary and Conclusion

A voluminous literature stemming from behavioral and molecular genetics, medicine, and neuroscience research has shown with a high degree of reliability that biology matters in the context of criminal behavior, drug-abusing behavior, and the nexus between the two. Several meta-analyses and reviews cohesively argue that half of the variance in antisocial behavior is genetically influenced (Barnes et al., 2014; Miles & Carey, 1997; Rhee & Waldman, 2002: Moffitt, 2005). Additionally, a large amount of literature has amassed showing how and which parts of the brain underlie antisocial behavior (Kiehl et al., 2000; Raine, 1993; Raine et al., 1994, 2000). Providing an explanation of how genes affect antisocial behavior is the understanding that brain structure and function are heavily influenced by genetic properties (Thompson et al., 2001). Genes influence how the brain forms and how it functions. In sum, variation in genes leads to variation in the brain, which, in turn, leads to variation in criminal and drug using behaviors (Beaver, 2009; Thompson et al., 2001). The brain, therefore, is the great mediator of human action.

Despite these points, biology is not deterministic. Bad genes and bad brains do not fatally prescribe someone to a life of crime and drug abuse. It is not possible to use biological indicators to perfectly predict criminal and drug abusing behavior (Aharoni et al., 2013). Half of the variance in criminal and drug abusing behaviors is due to biology, but half of it is not. The other half is explained by environmental influences. This point raises many important questions such as whether humans are "free" to choose their behavior (Harris, 2012) and whether criminal and drug abusing behaviors should be punished as harshly as they currently are (Raine, 2013). We leave these questions open for our colleagues to consider and debate.

So, what does this all mean? What do we do with the information about biological influences on criminal and drug using behavior in terms of policy? There are two competing (and extreme) interpretations. On one side is the argument that because a

person has no control of their biology then that person is less culpable for their crimes and thus punishments should be less severe or even avoided. On the other side is the argument that people afflicted with biological risk represent a danger to society and should be preemptively incarcerated, sterilized, lobotomized, etc. This dichotomy highlights some of the potential problems associated with figuring out how to utilize biosocial research to advance policy because both represent a misunderstanding of biosocial research. Criminal behavior occurs at the intersection of biology and the environment. In other words, genes are not the whole story and neither is the environment. Both are necessary to understanding how the brain functions, how it interprets social stimuli, and how complex human traits like antisocial behavior emerge. Perhaps the most important point is that through environmental interventions, biological risk can be moderated (see the above section on drug treatment) (Barnes, 2013; Rocque, Welsh, & Raine, 2012).

In the end, there is evidence to suggest biosocial research can lead to innovative responses to crime and drug use in modern society. Only after we achieve an understanding of the neurological pathways that are implicated in antisocial behavior will we be able to develop effective policy and more effective treatments. It is our hope that this review will encourage criminological scholars to seek out the volumes of evidence in disciplines that have, until recently, lived on the fringes of the criminological landscape. Specifically, we hope that this article will spark a discussion among the criminology and criminal justice community about the merits of neuroscience in the study and response to drug using behaviors among criminal offenders.

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