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Discovering Addiction

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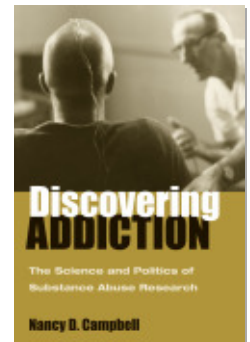
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CHAPTER 8

“The Hijacked Brain”: Reimagining Addiction

When President George Bush officially proclaimed the 1990s the Decade of the Brain, he stated the value of brain research for the U.S. war on drugs, “as studies provide greater insight into how people become addicted to drugs and how drugs affect the brain.” He explained, “These studies may also help produce effective treatments for chemical dependency and help us to understand and prevent the harm done to the preborn children of pregnant women who abuse drugs and alcohol.”¹ Tilting steadily toward neuroscience by the 1990s, the Decade of the Brain raised the public awareness, social status, and cultural capital of the field. As the brain became the “target organ of addiction” (DuPont 1997, 93), drug addiction, dependence, or abuse was redefined as a chronic relapsing brain disorder, a unified framework for a problem-based field in conceptual disarray. The laboratory logics by which addiction was localized to the brain dislocated it from the rest of the physical body and from the social body. These laboratory logics strategically borrowed the technical resources and social authority of neuroscience to garner new conceptual and political resources for the substance abuse research enterprise.² Although the borrowing strategy alienated some in the treatment community, it raised the profile of the research enterprise and enabled new forms of scientific learning.

Several preconditions had to be in place for neuroscience to “hijack” the field of substance abuse research. “The Hijacked Brain” was the title of the second part of a series narrated by Bill Moyers called *Moyers on Addiction: Close to Home*. The part aired on March 29, 1998, in the midst of public revelations of the heroin addiction of Moyers’s son. The hijacking metaphor conveys how

forcefully the brain is held "hostage" to drugs of abuse (Bloom 1997, 15).³ It was used to characterize what drugs of abuse did to the brain: "We have learned how some drugs and alcohol can disrupt volitional mechanisms by hijacking the brain mechanisms involved in seeking natural reinforcement and weakening brain mechanisms that inhibit these processes" (Volkow and Li 2005, 1429). The travels of the hijacking metaphor—and its staying power—forcefully convey how neuroscience remade the social worlds of substance abuse research with the claim that addiction was a chronic relapsing brain disorder. The implication was that the elusive secrets of this "disease of the will" would now yield to the powerful force of brain science.

Visualization of the long-hypothesized opiate receptors and the technical capacity to image the brain *in situ* created a new optics that made plausible the neuroscientific claim that addiction results when neurobiology goes awry. Opiate receptors, the molecular sites where drugs accomplish their work in the brain, were quickly mapped according to location and density. Neuropharmacologist Michael Kuhar explained: "A receptor is a place where a drug works. Receptors are all over the brain. You take a drug orally, get it in your stomach, then the blood carries it to the brain, bam, the drug sits in a receptor, and that receptor is activated" (2005). Here, individual cells are represented as actors in the dramas of pleasure and pain that underlie patterns of social interaction and cultural life.

Neuroscience gave substance abuse research the stamp of legitimacy, which was particularly important when NIDA faced becoming an NIH institute in 1992. Attracting neuroscientists raised the social and scientific stature of the enterprise, but it was a double-edged strategy that reduced the recognition that addiction is a complex disorder consisting of socially situated behaviors that occur within the particular cultural and economic geographies that shape which drugs are available to whom for what price. Although neuroscience has made legible "new modes of embodiment" (Wilson 2004), the ascension of neuroscience and genetics has also suppressed behavioral and sociological approaches better attuned to persons living with addictions. However, genetic, neurobiochemical, and behavioral approaches need not be mutually exclusive or opposed to one another. There are differences between, on the one hand, scientists already in the field of addiction research who, to advance knowledge about substance abuse, instrumentally took up new tools and techniques (e.g., positron-emission tomography [PET] scanning; functional, or "fast," magnetic resonance imaging [fMRI]; or cloning) and, on the other hand, scientists who saw the substance abuse arena as yet another arena in which to display

what these new tools and techniques can do. The latter have little historical connection to substance abuse research or pharmacology and low regard for both. The former have an instrumental interest in putting new tools in their place without attributing too much power to them or to explanations based solely on their deployment.

Outside the addiction research enterprise, neuroscientists viewed incursions from other fields with cynicism. A developer of PET scanning remarked:

I have had many people express an interest in using PET, typically established scientists in many fields who may be on a downhill curve of their career. Very overtly they express that PET is such a high road to science that they're willing to get involved now. They kind of held back before, but now they are willing to get involved because it is obviously so easy! They lack an understanding of what is entailed, I think, because the data comes out as pretty pictures. (Quoted in Dumit 2003, 57)

Indeed, many of my pharmacologist interviewees began to use these techniques late in their careers, after other approaches had proved inadequate. They learned how to work with PET scanning, genetic data banks, or microassays as the techniques came on line. Outsiders still construct pharmacology as merely an “acting accountant” of the pharmaceutical industry. Michael Phelps, one of the founding fathers of PET scanning, explained his view of the relationship between pharmacology and neuroscience as follows:

Pharmacology as a discipline began to fail in many ways. . . . If you go back about three decades ago, [when] pharmacology began, the major activity in pharmacology was neuropharmacology. It was a time of grind and bind, doing assays of neurotransmitter systems. That is how neuropharmacology became very popular and very productive. It was teaching a lot of new things about the brain, and drug companies had focused on the brain and were developing drugs for the brain. And pharmacology became the acting accountant for that. But then neuroscience was born, and neuroscience in a decade went from a group of maybe twenty-five, thirty people to fourteen thousand [by going into other disciplines] and collect[ing] out the neuroscience people. Well, in pharmacology, that was particularly devastating, because the best and the majority of people were neuroscientists. . . . [P]harmacology started to lose its way. . . . The industry was moving a lot faster than pharmacology was. It was lagging behind. (Quoted in Dumit 2003, 183–84)

Haunted by second-class citizenship, the modesty of the pharmacological sciences contrasts to the overpromising hubris of neuroscience, which echoes the optimism described at the beginning of chapter 4 in the present book. Yet

neuroscience simply does not explain enough of the complex social phenomenon that is addiction to be completely satisfying. Telling the story of how addiction became a brain disease as one in which neuroscience displaced all other approaches does not quite fit the data or the ethos of scientists who have spent their lives laboring in this field. A more accurate sense of the material conditions and thought constraints within which scientific labor yields scientific claims can be obtained by looking at how particular commitments and logics are embedded in practices, techniques, and technologies. Behind today's neurobiological models lie the shadowy outlines of perennial beliefs about drugs and drug users that shape their innermost experiences, as well as external observations of their behaviors. Neuroscience entered substance abuse research not as a revolution but as a legitimizing force deeply interconnected with behavioral antecedents and with Abraham Wikler's work on conditioning and the role of cues in triggering relapse.

Neuroscientific concepts of addiction emerged as the result of tools and techniques initially developed to visualize opiate receptors and trace their exact locations in the brain. These techniques and the conceptual advances they enabled profoundly changed scientific research on drug dependence. While neuroscientists have moved toward modular theories that "delocalize" capacities and show the diffusion of receptor sites, popular depictions relentlessly "localize" specific functions to particular locations in which the brain is the central actor (Wilson 2004, 93–94). Neurobiological claims are used in public discourse to stabilize a particular set of claims about innate differences and irreversible alterations of brain structure and function. Yet most neuroscientists in the substance abuse field have a considerably more multiple and elastic view of brain structure and function than public discourse admits. Today's neuroscience and molecular genetics are far from the reductionistic or deterministic endeavors of some of their historical antecedents.⁴ Yet they are still viewed with some suspicion. Whether neuroscience is depicted as in a state of underdevelopment or arrested development or as on the cutting edge, it is evident that it has not yet reached anything resembling a settled consensus on substance abuse or drug treatment.

REDEFINING ADDICTION AS A CHRONIC RELAPSING BRAIN DISORDER

People interpret their innermost sensations through the dominant lexicons of their time, which are often based on scientific scripts that have diffused

through social space. The earliest constructs of addiction as a chronic or relapsing disorder were not neurological. Starting in the 1950s, they were by the Public Relations Office at Lexington to explain high rates of release among those treated at the institution. The 1965 edition of Goodman and Gilman's *Pharmacological Basis of Therapeutics*, the monumental textbook for clinicians on drug action and drug-disease interaction, contained the following words in the chapter on "Drug Addiction and Drug Abuse": "In extreme forms, the behavior [compulsive drug use] exhibits the characteristics of a chronic, relapsing disease" (Jaffe 1965, 285). Having been asked to write the chapter by Alfred Gilman, who chaired the department of pharmacology at Albert Einstein, Jerome H. Jaffe had been a "two-year wonder" at Lexington and was on the cusp of embarking on a career to place science and treatment evaluation at the base of drug policy. Jaffe neither constructed drug addiction or abuse as a "brain disease" nor referred to anything but its most extreme forms as displaying the characteristics of a chronic, relapsing disease. The discursive shift to a "chronic, relapsing *brain* disease" came about in the 1990s. For instance, the now defunct Office of Technology Assessment (OTA) repeatedly asserted throughout a 1990 report, *The Effectiveness of Drug Abuse Treatment*, that drug abuse was a chronic relapsing brain disorder (CRBD) with "patterns of relapses and remissions that resemble other chronic diseases, such as arthritis and chronic depression." Written in the context of the HIV/AIDS epidemic,⁵ the report framed the "fatal link between the two epidemics" as fueling the HIV/AIDS epidemic due to the heterogeneous and unmarked population from which drug abusers were drawn (OTA 1990, 1).⁶ The OTA report suggested that a lack of rigor, unsophisticated design and analysis, "anecdotal, uncontrolled studies," and "poor study methods" pervaded the addiction research enterprise. Focusing on the need for comparative treatment evaluation, the OTA suggested "dissecting" programs to determine which components were effective for which client groups and custom fitting treatment to individuals: "Ultimately, research on drug abuse treatment should lead to what has been a common practice in medicine, namely a case management approach with an individual tailored plan to maximize the likelihood of treatment effectiveness" (1990, 10). The OTA favorably cited NIDA for embarking on randomized clinical trials, which would gradually displace disparaged forms of social, behavioral, and cultural research.

Translating between the specialized domain of neuroscience and the popular realm required a compelling figure. The "hijacked brain" was a condensed ideogram for the minute biological changes that manifested in the social phenomenon of "compulsive, uncontrollable drug use." Alan Leshner, director of

NIDA from 1994 to 2001 before becoming head of the American Association for the Advancement of Science, was the leading proponent of the discursive move to replace old ideology with the new science of the hijacked brain. A self-described "science guy," Leshner was beloved by audiences mesmerized by his "tough-guy swagger" in the town meetings through which he brought the concept of the CRBD to the field (Kreeger 1995, 12).

Central to the CRBD concept was the idea that neurochemical changes caused fundamental alterations in the brain that, as Peggy Orenstein reported, led to "drug-seeking becom[ing] as biologically driven as hunger, sex, or breathing." Orenstein continued, "Long after the addict quits, some of those brain changes remain, creating vulnerability for relapse" (2002, 6). The claim that vulnerability to addiction is a basic, biological drive to which some are genetically predisposed might be put to a variety of political uses, as could the idea that compulsive drug use fundamentally alters the brain.⁷ Defining addiction this way cemented neuroscience as the dominant approach to its study. This problem definition was then translated to a treatment workforce typically described as "backward," scientifically illiterate, or inadequately professional.⁸ The result was that those who enrolled neuroscientists in substance abuse research alienated frontline treatment providers, who were, until recently, often drawn from the ranks of addicted persons. However, Leshner was charismatic for treatment providers, who became friendlier to the science he embodied and still recall being transfixed when they listened to him (Bunk 1998, 1–2). The concept of the CRBD helped close gaps between the "science guys," the treatment community, and a public widely subscribed to recovery discourse.

Figuring addiction as a brain disease at the fundamental level finessed myriad differences within the research and treatment enterprise. NIDA could not monologically proclaim neuroscience as the one best way to understand addiction, given the dominance of behavioral pharmacology within substance abuse research at the time. Concessions to the effect that substance abuse is a social and behavioral process still had to be made. As Leshner stated in a 1997 article in *Science*, addiction is "not *just* a brain disease" but the result of a welter of environmental and historical factors. Proclaiming to viewers of Moyers's "The Hijacked Brain" that no singular approach was likely to yield adequate knowledge of the "most complex phenomenon that's facing our society," Leshner declared—and NIDA insiders echo him with little irony—that a thousand flowers would bloom at NIDA. He explained: "We need to bring a multidisciplinary approach to this problem, and that's what I hope the science will give us."

A thousand flowers did not in fact bloom at NIDA. Neurobiological models were pitted against social research and behavioral models, a struggle that took place barely beneath the rhetorical surface of the Decade of the Brain. A well-established drug ethnographer put it: “[T]here’s a lot of flowers blooming, but the ones that get cut and placed on the main table are very different. . . . Findings do not get disseminated in the same way. There’s all kinds of areas that we could be looking at, like controlled drug use, like harm reduction, like recreational drug use that [I just don’t see happening] in the political climate that I’ve been functioning in since I’ve been doing this work” (Murphy 2003). Similar complaints arose from geneticists and behavioral pharmacologists who felt cut out of the action by the redefinition. Privately skeptical of the assumptions behind the assertion that addiction was a CRBD, many conceded the usefulness of Leshner’s attempt to unify the highly differentiated interdisciplinary field of which he had assumed the helm, especially for raising its social status. The ascendancy of neuroscience, they agreed, was a necessary, if not inevitable, step to maturity.

Concerns about the field’s maturity arise periodically. In the mid-1990s, they led to the formation of the National Academy of Sciences Committee to Identify Strategies to Raise the Profile of Substance Abuse and Alcoholism Research, which in 1997 reported that the endeavor was a “mature field that should attract the very best scientists in both basic and translational research” (49), although it was largely failing to do so. The Institute of Medicine’s 1996 review of NIDA’s research portfolio proposed an agenda to ensure wiser public investment in drug abuse research (30–31). The consensus was clear—the field should court high-status neuroscientists (who were not yet occupying the field in great numbers) and also should perhaps invest further in genetics.

Advanced during the Decade of the Brain, the redefinition of addiction as a matter for neuroscientific investigation was more than a cynical ploy for appropriations. Once the word *brain* had been inserted into the phrase *chronic relapsing disorder*, neuroscience became the chief reference point. Beyond rendering addiction research a neat, tidy, and clean enterprise, the chief stake was the strong differentiation of addicted brains from nonaddicted brains. “The Hijacked Brain” cast neuroscientists as heroic “archeologists of the brain” united in their quest to unravel the “mysteries of the addicted mind,” mounting “extraordinary scientific expeditions to explain how some people will sacrifice everything to satisfy their hunger for a chemical fix” by showing exactly “how drugs enter pathways of the brain and how they alter the brain to create something that didn’t exist before.” The film depicted neuroscientists at

Massachusetts General Hospital using PET scanning technology to get a picture of "Denise," an African American cocaine user. The white-coated researchers complimented their subject—who is not "Denise" but her "nice lookin' brain"—and enacted the careful choreography that went into producing a "map of her feelings" when she is high. Claiming to see exactly "where craving for the drug actually takes place" as the drug was coursing through her veins, Steve Hyman, then the head of the Harvard Interfaculty Initiative on Mind, Brain, and Behavior and later director NIMH, interpreted the resulting image as one of "desire in the brain."

Leaving aside issues of interpretation and lack of standardization in the analysis of these images (issues pointed out in Dumit 2003), Hyman's use of the word *desire* signaled an older lexicon of addiction. At stake in the CRBD construct was the degree to which differences between addicts and nonaddicts could be characterized in terms of neuroanatomical brain signatures, neurochemistry, and neurogenetics and how long such differences endured. Leshner put it tautologically in "The Hijacked Brain": "It's a disease because it's the result of drugs changing the brain in fundamental and long-lasting ways. . . . [I]t's actually a different state." The debate was over the relative permanence of that different state. Leshner offered a haunting characterization of addicts: "Imagine being in a state where the drug has totally taken over their being; what that means clinically is that they're in a condition where they suffer from compulsive uncontrollable drug-seeking and use." Leshner was not in the addiction field; he had to be recruited to it, and reports have it that he was a hard sell because stigma pervaded his own structures of belief. As he did in "The Hijacked Brain," he would publicly say such things as "Stigma is one of the biggest problems for us in dealing scientifically with addiction," "People hate addicts," or "People are nervous that an addict is going to do something to them." The CRBD construct was supposed to banish stigma once and for all, a feat quite unlikely in American society, given the racial, ethnic, and class stratification evident in the history of drug use and drug policy. Instead, a neuroscience of difference is likely to simply become a way to render social and economic distinctions scientific.

There is a similarly repetitive pattern of claiming fundamental differences and asserting their inevitability in the neuroscientific approach to sex differences. Taken together, these beliefs converge on the long-standing notion that women are more biologically vulnerable to addiction and even further gone as a species of addict (Campbell 2000). An African American woman who appeared as a recovered heroin addict in "The Hijacked Brain" took up a common rhetorical role for women when she stated, "You don't feel like a human

being when you do drugs because the things you are doing are inhuman—you lie, you cheat, you steal.” Those are, of course, relatively human activities, but the point is that racialized female addicts serve as a condensed and potent metaphor for social decline. The figure of the addicted woman encodes compulsion without control, failures of self-governance, and the overwhelming power of illegitimate desires and insatiable needs. Because prevailing views of citizenship include the notion that only those who can govern themselves are fit to govern others, there are huge political stakes embedded in the claim that addicts’ brains differ fundamentally from nonaddicts’ brains.

Conceptual definitions work as technologies of visibility to channel attention and resource allocation in scientific research. External depictions of addiction science cast it as deeply riven with questionable approaches and results (Institute of Medicine 1996 and National Academy of Sciences Committee to Identify Strategies 1997). Moves to portray the results of addiction research as unequivocally known rather than unknown do not take place in a sociocultural vacuum. Historians have shown that the margin of social tolerance for addicted persons depends on how members of the dominant classes perceive them. Because scientific constructs perform cultural work within institutions, such redefinitions affect the governance of drug use and drug users. A nagging sense remains that addiction is not just a brain disease and that neuroscience is not quite enough to erase the traces of the cultural repository of ideas and images that underlie assumptions about the essential ungovernability of drug addicts.

“THIS IS YOUR BRAIN ON DRUGS”: THE BRAIN BECOMES A MATERIAL-SEMIOTIC ACTOR

Claims issuing from behavioral pharmacology and neuroscience differ in the cultural work that they perform. By defining drugs as reinforcers, behavioral pharmacology leveled social distinctions between organisms who use drugs of abuse and those who do not. In the United States, neuroscience, in contrast, has been pursued as a science of difference and used to reinscribe social hierarchies.⁹ Relationships between the new old-timers (the self-proclaimed radical behaviorists described in the previous chapter of this book) and neuroscientific newcomers were sometimes tense. Michael Kuhar explained: “Drug self-administration had captured people’s imagination very, very much like receptor binding had. The thing about drug self-administration, one of the things that I think people overlook, is that it really was another paradigm shift because

it showed that animals will take drugs. There's nothing intrinsically bad about this animal or that animal. That was a very important paradigm shift for treating drug addicts. It was clear that taking drugs and seeking drugs was a capability of everybody's brain" (2005).

When neuroscience became useful in the addiction research enterprise, behavioral pharmacology was the dominant approach. Neuroscientific newcomers remember being treated like "redheaded stepchildren." Coming from physics and mathematics, they had misgivings about whether behavior was "a rigorous science": "Instead of looking at a moving, behaving animal and observing how much drug they were taking, we were looking at the molecular site where that drug acted. We were stepping into a new microscopic realm of drug action and drug taking" (Kuhar 2005). When the opiate receptors, the main nonhuman actors of that microscopic realm, were first visualized, few established addiction researchers were studying the brain, and those doing so used *in vitro* and *in vivo* techniques. They were divided over whether receptors or single-molecule binding sites were "real" or not. Among believers, there were those who thought there were multiple opiate receptors and those who did not.

Michael Kuhar's career trajectory provides a sense of what it was like to work in a field going through profound conceptual, technical, and discursive shifts every decade or so. Upon entering the field in 1973, Kuhar was scolded by a professor at a prominent university for "talking about receptors as though they were real": "He said that everybody knows receptors aren't real. They're mental constructs that we use to think about how drugs work." Kuhar's first "NIDA" grant came from ADAMHA in 1972.

There weren't drug receptors at that point, and we didn't know how drugs worked. There was no cloning. We didn't understand the molecular biology of brain proteins very well. The drug self-administration model, that behavioral model which is very important in the field, had really just become established. There was no PET scanning then. There was very little or no brain imaging then. There were few brain banks. I was one of the first individual investigators to have a brain bank, a repository, actually a freezer, where brains are kept for experimental purposes. . . . The patient from which the brain was taken is well documented in terms of his medical history, whether or not he's an addict or she's an addict. (Kuhar 2005)

Evolution of the technical means for studying the brain without access to post-mortem human tissue, a scarce and contentious commodity, expanded capacity for neuroscientific research. Nonradioactive methods expanded that capacity once again.

The highly publicized visualization of opiate receptors, the molecular sites of action often described through the metaphor of a lock and key, ushered in an era of “receptor fever.” Long a hypothetical entity, the receptor came into theoretical existence well before it could be visualized. As early as 1913, Paul Ehrlich described how toxins injured cells: “They are absorbed by certain specific component parts of the cell side chains which I have characterized as ‘receptors’” (quoted in De Jongh 1964, xiii–xvi).¹⁰ Somewhat later, he wrote: “Only such substances can be anchored at any particular part of the organism, as fit into the molecules of the recipient complex like a piece of a mosaic finds its place in a pattern” (quoted in Ariens 1964, xiv). The 1960s elaboration of a science of molecular pharmacology (the systematic knowledge of interaction between body and drug molecules) stands as a singular example of prescience or—in another, more masculinist lexicon—Nature unveiling herself: “To most of the modern pharmacologists the receptor is like a beautiful but remote lady. He has written her many a letter and quite often she has answered the letter. From these answers the pharmacologist has built himself an image of this fair lady. He cannot, however, truly claim ever to have seen her, although one day he may do so” (Ariens 1964, xvi).¹¹ The feminization of the receptor is inescapable in this passage, which relies on a courtship metaphor long associated with the discourse of Western science.¹²

Elucidation of the opiates’ chemical structure led to postulation of receptors in the mid-1950s. However, technologies for locating, purifying, or visualizing receptors had not yet been developed.¹³ In the 1960s, several laboratories made unsuccessful attempts to locate and isolate receptors (Cozzens 1989, 68–69). Unable to purify the receptor in 1969, Avram Goldstein nevertheless demonstrated stereospecific binding at the opiate receptor site in 1971 in the membranes of mouse brains. He is not credited with discovering opiate receptors, since Candace Pert and Solomon Snyder exerted a stronger claim to have shown actual receptors, not just binding sites, in 1972 (Cozzens 1989). Soon after, John Hughes and Hans Kosterlitz discovered the endogenous opioids that they named *enkephalins*. The myriad implications of these multiple discoveries ranged from the popular reconfiguration of ideas about body and brain to the production of a “common language for psychiatry and the pharmaceutical industry,” which brought them into alignment rather than competition (Healy 2002, 212–15).

Once visualized, receptors could then be located by using autoradiography, to study their distribution and density in monkey and human brains. Kuhar observed: “At that point, the immediate world started working on receptors.

Very quickly, receptors for all the major drugs of abuse were discovered: there were the serotonin receptors for LSD; there were all the opiate receptors for opiates; [there were] barbiturate binding sites, or GABA receptors" (2005). Among the technical limitations was the need for postmortem brains, until PET scanning enabled noninvasive study in a way that researchers experienced as "almost like Alice in Wonderland." Kuhar put it: "There was an old Chinese mythological figure called Shen-Nung [who] was a physician who had a magical power. He could ingest an herbal medicine, make his body transparent, and then he could point to where the drugs were working. Here we were with PET scanning, showing where drugs were working as if we had made the body transparent, which of course we had! It was an absolute fairy tale come true" (2005).

It is hardly remembered as well that ARC research director William R. Martin had hypothesized the existence of multiple opiate receptors in the mid-1960s, when Lexington was in its heyday. Frank Vocci, head of the NIDA Medications Development Division from 1995 to 2003, explained: "Martin's conclusion was that when you look at the whole body of research on the opiate receptor, it can't just be one receptor. He said there had to be more than one opiate receptor. He was actually the first guy who deduced this from pharmacology data. What happened in the mid-seventies was that you had people who started to look at what these multiple receptors were from the standpoint of radio receptor binding, and to then find endogenous ligands for them. This was during a really exciting basic science explosion that was occurring in terms of the neurochemistry of all this" (Vocci 2005). Propelled by development of neuroimaging technologies, this discovery period was a technique-driven scientific process through which receptor location and density was mapped. Candace Pert wrote, "My method was to develop a technique and then ask all the questions to which the technique could supply an answer" (1997, 128).

The imagery of "photoneurorealism" (Pert 1997, 126) not only yields pretty pictures but has practical applications for drug development and screening. The pharmaceutical industry uses PET scanning to determine exactly which receptors a drug occupies, a relatively noninvasive way to screen compounds by determining the molecular profile of action, predicting likely side effects, and determining clinically effective dosages.¹⁴ As Kuhar explained, substances compete for receptors: "When you inject radioactive morphine, morphine sits in that receptor but it's competing for the endogenous ligand. It's competing for opioid peptide. Another thing that PET scanning of receptors gave us was a way to measure endogenous activity because there would be a competition

between endogenous substances and the radioactive drug” (2005). The relative success of one compound over another in this competition provides a high-throughput drug-screening method. But PET scanning also enabled a neuroscientific rehabilitation of pharmacology and the legitimization of substance abuse research as a domain of neuroscience.

Public sector science sensed that the frontier of drug abuse research was moving, so NIDA inaugurated its Neuroscience Division in 1985, choosing Kuhar to head the overall division and one of the four laboratories in it. The division, which included a genetics laboratory headed by George Uhl, embarked on a quest to find out whether there were structural and/or functional differences between the brains of addicts and nonaddicts. One of the first important breakthroughs was the isolation and cloning of genes for dopamine receptors, which ushered geneticists into the inner sanctum of the substance abuse research enterprise. Another important moment was development of the technical capacity for signal transduction. Kuhar explained: “When a drug binds to a receptor, there’s a whole bunch of things that happen inside the cell. That’s called ‘signal transduction,’ changing the signal from a chemical binding to a whole series of biochemical reactions inside the cell, [which] involve[s] changing gene expression, and changing the genes that are turned on” (2005). The convergence between genetics and neuroscience yielded new conceptual and technical approaches that rendered many previous approaches obsolete. For instance, the kind of drug abuse liability studies once done on the monkeys of Michigan or the postaddicts of Lexington are accomplished today by molecular pharmacologists using single-cell preparations onto which cloned opiate receptors are grafted. This technique allows far more accurate measurements of the affinity that a particular compound has for opiate receptors, and researchers who work on intact organisms are free to work on other problems.

Remaining in the problem-based field of addiction research requires disciplinary mobility. As Kuhar explained, neuropharmacologists had to learn much in order to incorporate genetics.

The actual nuts and bolts of cloning, for example, involved technical things called plasmids, vectors, recombinant enzymes, a whole series of things that existed in other fields, that hadn’t been brought into neuropharmacology. These were now being brought into neuropharmacology. We had to learn what the hell they were. How do you handle them? How do you store them? How do you make one? How do you know when you have one? How do you know when it’s not working properly? How do you know if it’s an artifact? So we had to learn all those things. (2005)

Software programs were among the necessary tools required to access the new gene depositories created by the Human Genome Project. Kuhar recalled: “We had to figure out how to use them. What do the words mean? A lot of that stuff was just coming out. It was clumsy. It was awkward” (2005).

Since departing NIDA in 1995, Kuhar has used the Human Genome Project to study a particular peptide neurotransmitter called the CART gene, a candidate gene involved in behaviors central to addiction. Describing his onetime skepticism toward both behaviorism and genetics, he said: “I didn’t think we could ever understand behavior. I thought behavior was so complex that we couldn’t really get a good handle on it. I don’t think that way anymore. Very, very complex behaviors can be shown to be dependent on a single gene.” Potential treatment applications are sought by using genes to blunt or modulate behavioral effects of drugs of abuse. Pharmacotherapies that work by blocking drug effects have found little popular acceptance among the addicted, despite their seeming elegance at the molecular level. Neurogeneticists explain lack of social acceptance by appealing to the idea that the “brain-reward system” is basic to survival. Kuhar said, “If you’re dealing with a system so fundamental as appetite and addiction, and they’re intertwined, blocking something so vital to our survival is not going to get so far” (2005). The construction of the brain as the central coordinator of this reward system comes out of James Olds’s work on electrical brain stimulation during the 1950s, which helped inaugurate behavioral approaches to self-stimulation and drug self-administration. The construction of the brain-reward system as crucial to the survival of the species has come about rather more recently. Substance abuse researchers construct their enterprise as fundamentally concerned with human evolution and ultimately useful in unmasking responses to pain and pleasure, mechanisms that regulate appetite and satisfaction, and the compulsion to repeat drug experiences.

As a central organizing metaphor, the brain-reward system transformed the old addiction research enterprise into the current substance abuse research enterprise by expanding the behaviors and substances—endogenous and exogenous—under consideration. Kuhar observed:

Just think about how many different kinds of medical morbidity are associated with the reward system. There’s not only drugs of abuse. There’s cancer because of smoking, liver disease because of alcohol, Type II diabetes because of overeating, cardiovascular disease because of body weight and food intake and all. While we think of the reward system as specifically related to drug addiction, it is in fact a major biological system in the medical field, underlying a lot of morbidity that goes way, way beyond drug abuse. (2005)

Repetition is the key to the brain-reward system, the existence of which, as Kuhar said, “reinforces certain actions [that] turn out to be things that are good for your survival—food, water, salt, sex.” Kuhar explained: “Those things are turned on by the reward system. If we didn’t have reward systems, we’d have been gone a long time ago. The reward system is the secret to life” (2005). Thus did a scientific enterprise once trained on marginalized, stigmatized “deviants” become a key to the very “secrets of life” (Keller 1992). More than a route to garner public support, the construction of the brain-reward system as the supposed secret to life has enabled scientists to justify their views on drug policy. As Kuhar put it, given the number of chemical compounds, “it isn’t surprising that some few are going to activate that reward system, maybe by mistake, just by chance.” He continued:

Those things are the drugs that turn out to be abuse drugs. They activate that reward system, the reinforcing system. Understanding that there is this naturally occurring system in the brain, the view of drug addiction has changed tremendously. It’s now physiologically based. This is a physiologically based brain disorder, like Parkinson’s disease, [and] we can develop medications now to treat these things. Treatment is a lot more effective and cheaper than incarceration. (2005)

The political perspective on the futility of incarceration is a convergent perspective among scientists who study drug dependence.

Genetically based explanations can lead to claims of persistent and even irreversible alteration, as in the following excerpt from my interview with Kuhar.

One of the other major discoveries goes like this. When you take a drug, the drug binds to receptors. The receptors are activated and then things happen inside the cell . . . because this receptor’s being activated. [T]herefore the brain on drugs is a different brain. It’s chemically different. It’s chemically changed. That’s a great realization because a reasonable strategy for treatment is restore the old balance, and you’ve got somebody unaddicted. I think that may be true. In other studies, there were other striking findings, and people didn’t believe it at first. It was found that these changes in the brain last a long time. We’re talking about months and months, maybe years. That’s why drug addiction is a chronic relapsing disease, because the changes that are caused are very long-lasting. (2005)

One reason for pausing to reflect before jumping on the neuroscientific bandwagon is that the approach leaves much to be desired when it comes to evolv-

ing treatment methods to cope better with relapse and recovery. Not everyone agrees that persistence of changes in the brain accounts for behavioral change. Eric Nestler and David Landsman explain:

The cardinal feature of addiction is its chronicity. Individuals can experience intense craving for drugs and remain at increased risk for relapse even years after abstinence, so addiction must involve very stable changes in the brain. But it has been difficult to identify such changes at the molecular, cellular, or circuit levels. The molecular and cellular adaptations related to tolerance, sensitization, and dependence do not persist long enough to account for the more stable behavioral changes associated with addiction. (2001)

The hope is that neuroscience will lead to understandings of how “cellular and molecular mechanisms . . . mediate the transition between occasional, controlled drug use and the loss of behavioral control over drug seeking and drug taking that characterizes chronic addiction” (Koob and Bloom 1998, 467). The idea that chronicity might be a feature not of the brain on drugs but of social worlds in which people learn to use drugs in chronic ways remains difficult for neuroscientists to grasp, because so few are in close touch with chronic drug users. The apparent triumph of neurogenetic approaches ought to be at least as troubling as earlier approaches. Happily, there are a few exemplary research groups that display a sense of historical continuity with the addiction research enterprise and a concern for close social proximity with research subjects.

BRINGING LIFE INTO THE LAB: THE SEARCH FOR THE “PSYCHE” IN THE NEUROIMAGING LABORATORY

Abraham Wikler’s scientific heir apparent, Charles P. O’Brien,¹⁵ learned to “superimpose research on good treatment” when he was drafted during Vietnam. He directed the Philadelphia Naval Hospital psychiatric unit between 1969 and 1971, during his medical residency. O’Brien recalled: “One of the major reasons for my patients being unfit for duty was because of drug abuse, which provoked other kinds of psychiatric problems. . . . I got interested because it was so clinically important, and there was so little science” (2005). O’Brien was then recruited to start a treatment program at the Philadelphia Veterans Administration Medical Center. Thus, during President Nixon’s 1972 presidential reelection campaign, O’Brien found himself running one of the first VA programs dealing with heroin-addicted veterans returning from Vietnam.

Describing his treatment program as “science-based” from its inception, O’Brien became interested in Wikler’s animal conditioning model. In 1977, he validated Wikler’s model by demonstrating that craving and withdrawal were conditioned responses in human beings. He began using addiction as a model for memory: “This is how we came to the idea that addiction is a chronic disease—because it’s a memory. It’s not a brain lesion, it’s a very much over-learned memory, like learning how to ride a bicycle or play the piano” (O’Brien 2005). When asked why Wikler, who had access to human subjects for much of his career, had not made the jump to thinking of addiction as a form of over-learned memory, O’Brien said:

He was very helpful to me because I wrote to him very early on and told him what I wanted to do. He wrote back and thought it was a great idea, but he only actually studied rats. He talked to people, but he only did experiments on rats. I was the first one to do experiments on human beings on this. Wikler had been influenced by Pavlov, who did the first work in conditioning of drug effects. . . . What I did, essentially, was design in Philadelphia something like they have in Russia. By coincidence, I got invited to Russia [in 1974] along with a VA delegation, and I visited some of Pavlov’s students, [but] by that time he was dead. (2005)

Like Pavlov’s lab in Russia, Wikler’s lab at Lexington took on new life in Philadelphia.

Near the end of his career, Wikler reflected on his long search for the “psyche” in drug dependence. He described how he had evolved his research plan from his first brush with Pavlov, who, having shown that decorticated dogs could not be conditioned, had concluded that the cerebral cortex was essential to development of conditioned reflexes. “Groping for an operational definition of the ‘psyche,’” Wikler inferred that if an organism could “learn, i.e. could acquire conditioned reflexes, it had a ‘psyche’; if not, then, no ‘psyche’” (Wikler 1974, 2). He transformed the problem into a puzzle to be solved via laboratory logic: by what practical techniques could the learning patterns of the “psyche” be made evident in a demonstrable way? By the 1970s, Wikler felt the clues were clearer than they had been when he had embarked on his quest more than three decades previously. Summoning the ghost of psychoanalyst Sandor Rado, Wikler closed his 1974 Nathan B. Eddy Memorial Award lecture before the College on Problems of Drug Dependence thusly: “Regardless of whether or not there is any validity in Rado’s dictum, ‘. . . not the toxic agent but the impulse to use it makes an addict out of a given individual,’ the evidence is

abundant that both the 'toxic agent' and the schedules of reinforcement under which it is self-administered are crucial in the development of the disease *sui generis* that is called drug dependence" (10).¹⁶ His hybrid integration of behaviorist and psychoanalytic lexicons was linked to new research, such as O'Brien's demonstration that "classically conditioned tearing, yawning, lacrimation, systolic blood pressure elevation, respiratory irregularities and skin temperature decreases can be developed in subjects maintained on methadone in response to conditioned stimuli such as an odor or a tone coupled with saline injection, after the odor or tone had been paired repeatedly with injections of naloxone, the unconditioned stimulus" (Wikler 1974, 10). Finally, Wikler spoke of a suggestive polygraph study in which postaddict subjects appeared to respond differently to opioid-related images than they did to neutral slides. Lamentably, the polygraph had broken during the study.

Polygraphs (so-called lie detectors) were initially employed by O'Brien's group to study learned responses to opiate cues by measuring arousal reactions. The idea fit into cognitive-behavioral therapy designed to teach people to extinguish arousal responses. Hired in 1981 to work with behavioral and polygraphic assessment of response to drug cues, Anna Rose Childress moved cue studies into the neuroimaging laboratory, adopting SPECT (single photon emission computed tomography) neuroligand imaging in 1991; PET scanning in 1996; and nonradioactive functional, or "fast," magnetic resonance imaging (fMRI), which can be used for longitudinal studies because the process does not use ionized radiation and therefore can be repeated in single subjects.¹⁷ Imaging technologies were adopted for the study of drug addiction because they allow noninvasive mapping of the neuroanatomical and neurochemical substrates of desire, or "appetitive drug motivation."¹⁸ The Philadelphia laboratory moved from studying opiates to studying cocaine. They produced data sets on drug craving, showing the activation of particular regions of the brain in response to videos depicting drug paraphernalia and visual images associated with local drug subcultures.

Neuroimaging technologies are useful for understanding relapse after long periods of not using drugs. Successive generations of imaging technologies have supplanted the polygraph's crude physiological measurements and today attempt to corroborate the physical changes that memory makes in the brain. O'Brien observed:

Clearly my patients have a memory that won't go away. When I show them cues that are associated with addiction, they develop craving; they have blood pres-

sure, pulse, and respiration changes. [W]e've been able to demonstrate that they have brain changes, which they can't control. So when they are in the brain imaging chamber, and we show them a video of people using drugs, there's a reflex that goes on. We see brain activation. It's not something that you can command off by just saying no. (2005)

Brain imaging experiments narrow in on the powerful urge to return to drug use. By bringing into the lab images of the everyday objects, sights, and sounds that cue research subjects that opiates may be coming, researchers are trying to visualize “emotional memories” that serve as triggers for relapse. In Moyers’s “The Hijacked Brain,” Childress referred to these “feeling memories” as powerful and long-lived memories that concern things that enhance survival. The purpose of her PET scan studies, Childress explained on camera, was mapping where such emotional memories are stored so as to develop signatures of craving in the brain. To accomplish this, she and her patients produce true-life videos to capture associations that trigger people to remember their feeling states when high. These associations are social cues—the persons, places, and things—said to trigger relapse in the lexicon of popular recovery discourse.

Neuroimaging studies did not completely displace behavioral study. In fact, Vocci describes fMRI as “married to behavioral tasks that people do in the magnet” (2005). Again, the social location and material conditions of the research site matter. The University of Pennsylvania Center for Studies of Addiction is connected to a treatment research institute and a treatment center that enable interactions between researchers and patients actively struggling to end their addictions—or, in the lexicon of those who study them, to inhibit their responses to social and environmental cues. Childress refers to the patients she works with as “collaborators” and relies on them to coach her research team on how to better induce craving “in the magnet” in order to study why craving persists “outside the magnet.” The process of bringing life into the lab replicates to some extent the social and material conditions available to the ARC when it was at Lexington. The original 1948 study that formed the basis for Wikler’s conditioning theory involved the experimental readdiction of a single human subject who shared his free associations, manifest dream content, and interpretations in psychoanalytic interviews two or three times a week for several months (Wikler 1948b, 1952d). Although this study could not be replicated today, cue-triggered responses from subjects undergoing neuroimaging similarly integrate behavioral and neuropharmacological approaches. Likewise, an fMRI cocaine study performed at Massachusetts General Hospital in Boston asked subjects who were regular, untreated cocaine

users to report their subjective states following a placebo injection and an injection of cocaine (Brieter et al. 1997). By correlating imaging data with subjects' rating of their state of "craving," "rush," "high," and "low" throughout an imaging sequence, researchers identified brain regions they believe are implicated in the subjective sensations experienced by cocaine users. Vocci explained:

[Neuroimaging studies have shown that] individuals' responses, what they felt, and what their brains were doing were not necessarily concordant, but the ones that got the highest response in their brain were the ones that relapsed. . . . [This] suggests that there are brain systems that are impacted by drugs of abuse to the point where, although the person looks just the same as somebody else who's gone through a treatment program and they're not using drugs at that time, their probability of relapsing is very high. The guy next to them who doesn't have that response is low. We've always wondered, why does one guy make it and the other one doesn't? From these technologies, it's starting to look like you might be able to pick these folks out during or after treatment, and say, this one's got a brain signature that's suggestive of relapse, and this one doesn't. (2005)

The hope that science will someday indicate which treatments might be effective for whom obviously has the downside of marking those on whom treatment would be a lost cause. For employers, parole boards, child protective services, and other authorities, this could easily become grounds for new forms of discrimination. At the same time, such a process, if fairly implemented, could be useful for channeling public health resources. However, there are as yet no practical implications resulting from this domain.

The outcome of neuroanatomical mapping is a "brain signature," which supposedly shows what is happening in the brain at a particular moment in time. Such images do not yield knowledge of the underlying neurochemistry necessary to develop medications. In fact, when O'Brien and colleagues tried to use cue-reactivity paradigms to screen medications supposed to block or blunt cue-induced cravings, their results were "underwhelming" (as explained on their Web site, cited in n. 18). They then strategically retreated from the goal, returning to basic research focused simply on understanding addictive states. What, then, does a brain signature do? Photoneurorealism provides a convincingly objectified map of subjective variation and is thus thought to hold the key to the long-pursued questions of addiction research: Why do only some people become addicts? Why do only some people relapse? Neuroimaging is today's version of the old attempt to render subjective effects objective and to hold at

bay questions of social and economic context. What will we do once we know the answers, and what will that knowledge be used to accomplish?

Rapid technological development of imaging technologies propelled a rush to embrace metabolic and physiological models of drug dependency. Sociological, anthropological, and psychological models have been displaced. Whatever addiction may be, the expert communities who deal with it in our time no longer consider it a social problem. Recently, social and cultural factors have paradoxically reentered through the backdoor of genetics. There are possibly fundamental barriers in the way of interpreting addiction as a primarily cellular process, rendering emotional motivations and behavioral expressions as purely molecular matters. First, there is little knowledge of how molecular events translate into cellular interactions and, so the story goes, into complex social behaviors. Second, there is little knowledge about the effects of long-term exposure, a critical component of a chronic relapsing disorder supposed to fundamentally alter brain structure and function. The CRBD construct itself drives research in a particular direction. Third, the potential contribution of genetics to vulnerability is admittedly poorly understood, although neuroscientific optimists pursue vulnerability genes and hope eventually to explain the role of genetic risk factors and protective mechanisms (National Academy of Sciences Committee to Identify Strategies 1997, 47). One need not argue against neuroscientific or genetic research in order to notice that the explanations so far offered share that most salient feature of all drug addiction research over the past century—they are limited, partial, and incapable of addressing the role of social context or integrating all levels of analysis.

In addiction research, a most public science, conceptual models provide answers to ongoing questions about what kinds of knowledge are most useful to govern drug use and drug users. By the end of the twentieth century, that answer was that social behavior can be understood through molecular means elaborating the neurobiochemical and genetic pathways that reward users and reinforce their behavior. What haunts this technoscientific construction of addicts as a fundamentally altered species structurally and functionally different from the rest of us? Leshner himself answered this question in a special, 1997 edition of *Science* magazine on addiction: “Addiction is not *just* a brain disease” (46). Its social meanings mark the presence of continued concerns with deviance or aberrant behavior that remain part of the cultural repository of ideas and images that underlie our assumptions about governance. Current NIDA director Nora Volkow refers to drug addiction as “disrupted volition”

(2006) or “behavior gone awry” (Volkow and Li 2004). Volkow and Ting-Kai Li observe:

Drug addiction manifests as a compulsive drive to take a drug despite serious adverse consequences. This aberrant behaviour has traditionally been viewed as bad “choices” made voluntarily by the addict. However, recent studies have shown that repeated drug use leads to long-lasting changes in the brain that undermine voluntary control. This, combined with new knowledge of how environmental, genetic and developmental factors contribute to addiction, should bring about changes in our approach to the prevention and treatment of addiction. (2005, 1430)

The wording of the preceding quotation reveals that continued activity of the old moral lexicon since the nineteenth century has constructed addiction as a “disease of the will” subject to voluntary control. The work of Volkow, Li, and other neuroimagers testifies to the convergence between behavioral and neuroscientific approaches in the study of what constitutes volition itself and what processes lead to “disrupted volition” (Volkow 2006). With that amnesiac gesture toward its own repressed past, the addiction research enterprise comes full circle into the present.

Redefining addiction as a chronic relapsing brain disease in the waning decades of the twentieth century provides a striking example of amnesia with which to close this chapter. Back in 1966, Warren P. Jurgensen, the deputy medical officer in charge of the Lexington Hospital, told the American Correctional Association that addiction was a “chronic, often relapsing affliction, which may require treatment intermittently for a period of years.” Like many at Lexington, he defined addiction as an “illness with relapses often to be expected,” adding: “It is believed that periods of abstinence can be lengthened, and in some cases extended indefinitely. Indeed, this is characteristic of the medical treatment of many chronic illnesses.”¹⁹ Although this problem definition did not stick in the 1960s, it preceded by decades the adoption of the strangely similar definition used to court neuroscientists to the field in the 1990s. Subject to cycles of learning, forgetting, and relearning, the social worlds of addiction research continue to face the intractability of the drug problem in the United States. How they will do so in the future owes something to the ways they have done so in the past.