Changing the Stamp of Nature:
Pornography Addiction, Neuroplasticity, and the ASAM and DSM Perspectives
Donald L. Hilton Jr., MD, FACS
The Society for the Advancement of Sexual Health (SASH)
September 21, 2012

It is a privilege to be with you today, and to have this opportunity to speak about this subject. Much of
the consternation regarding whether compulsive destructive sexuality is an addiction or the child of
some lesser god, some milder malady, likely relates to how we define the term itself. The earliest use
of the word in English by Frith in 1529 in Antithesis was based on the Latin addict-us: “assigned by
decree, made over, bound, devoted.”¹ Shakespeare first used the word “addiction” in Othello, “Each
man to what sport and revels his addiction leads him.”² In describing lust Shakespeare also described
sexual addiction in Sonnet 129; it reads as if it had been specifically written to describe pornography
addiction:

The expense of spirit in a waste of shame
Is lust in action: and till action, lust
Is perjured, murderous, bloody, full of blame,
Savage, extreme, rude, cruel, not to trust;
Enjoyed no sooner but despised straight;
Past reason hunted; and no sooner had,
Past reason hated, as a swallowed bait,

² Othello, Act II, ii 6
On purpose laid to make the taker mad.
Mad in pursuit and in possession so;
Had, having, and in quest to have extreme;
A bliss in proof, and proved, a very woe;
Before, a joy proposed; behind a dream.
All this the world well knows; yet none knows well
To shun the heaven that leads men to this hell.

The first recorded use of the word addiction in a medical context was a remarkable statement in the Journal of the American Medical Association that is as true today as it was in 1906: “It matters little whether one speaks of the opium habit, the opium disease, or the opium addiction.” This statement is also true whether it refers to opiates or to sex. In 1983 Dr. Patrick Carnes coined the term “sexual addiction” based on behavioral parameters. Others have supported this behavioral model for sexual addiction: consider, for instance, the recent paper by Garcia and Thibaut: “The phenomenology of excessive nonparaphilic sexual disorder favors its conceptualization as an addictive behavior, rather than an obsessive-compulsive, or an impulse control disorder.” Psychiatrists such as Dr. Daniel Angres at Rush Medical School and Drs. Bostwick and Bucci at Mayo Clinic also support the concept of compulsive sexual behavior as being addictive. Angres and Bettaniardi-Angres defined addiction as “the continued use of mood-altering addicting substances or behaviors (e.g., gambling, compulsive sexual behaviors) despite adverse consequences.” In addition to behavioral perspectives, a biological perspective of addiction has emerged in the last decade, one which defines addiction as a chronic disease of the brain affecting the reward, motivation, and memory systems.

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3 JAMA, March 3, 642/2, 1906

6 Science 6 July 2007; Vol. 317. no. 5834, p. 23
and which combines both substance and behavioral addiction under a common umbrella, culminating in the ASAM definition of August of 2011. Sexuality can therefore, in this biological model, become addictive. Rather than focusing on whether the addictive behavior involves drawing a syringe or clicking a mouse, addiction involves and alters the biology, and the biology then affects subsequent behavior. Addiction neuroscience is as much about neuronal receptors as it is destructive repetition.

There are currently no prospective peer-reviewed studies on pornography or sexual addiction, for that matter, in the context of neuroscience. Truly unbiased research on human sexuality is probably not possible in today’s cultural environment, particularly given the financials. At 100 billion dollars a year porn is big business, to say the least. Pro-porn activism has ensured that any true research regarding unrestricted sexuality will take place in a scientific vacuum. Any attempt to present unlimited sex as harmful is immediately scripted as Victorian moralistic prudishness, an infringement on First Amendment rights. That the discussion might venture into biological and/or demographic effects therefore never becomes an issue. As long as condoms are secure and viruses are contained, any sexual activity is thereafter ‘safe’ with no possible emotional, behavioral, or especially, addictive effects.

The porn industry’s 100 billion dollar reason to fight the addiction label is obvious, and is given voice by one industry representative:

While much has been written and said about pornography being addictive, on par with drugs, booze and cigarettes, it's important to consider that this misinformation has been based upon questionable “science” and the opinions of anti-porn activists -- not upon any legitimate, unbiased research. Consider also the fact that "drugs, booze and cigarettes" are all physical,

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7 ASAM Long Definition
chemical agents that are ingested and can indeed have measurable, harmful, addictive effects. The mere viewing of any type of subject matter hardly falls into this category and, in fact, belittles the very real battles that addicts face over drugs, booze and cigarettes -- all of which can be lethal. No one ever died from looking at porn. While some compulsive types can be "addicted" to anything, such as watching a favorite television show, eating ice cream or going to the gym, nobody suggests that ice cream is akin to crack cocaine and should be regulated to protect...people from themselves -- instead, these compulsive actions are rightfully viewed by society as personality defects in the individual...  

An example of this same perspective manifest as academic apologism with regard to human sexuality is seen in a recent article in Salon. The author of the article trumpets a succession of psychologists who support some variant of the same statement “There is no specific study on pornography showing any effects on the brain.” For instance, one said, “Not even a smidgen of such evidence exists...,”

Understand that by “evidence” they mean a prospective double blinded control where, as one Salon article source said, we would have to take two cohorts of children, expose one to porn and protect the other to prove causation. Obviously this won’t happen given the ethical issues with such a study. Yet I would presume that these same psychologists would accept the premise that tobacco is addictive without demanding the same prospective, child-based study. In other words, where is the comparative prospective study with tobacco in children? The one that divides the kids, gives half cigarettes, protects the others, and follows them? It doesn’t exist, of course, and never will, and therefore those so biased will still say that smoking is not addictive, even now. So said the seven tobacco executives in front of Henry Waxman’s subcommittee on Health and the Environment. In succession, each said “No” when asked if smoking was addictive.

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9 Santorum’s Bad Porn Science, Salon, March 20, 2012 http://www.salon.com/2012/03/20/santorums_bad_porn_science/
Yet based on a tapestry of research over the decades virtually everyone but these tobacco executives believes evidence exists that tobacco is indeed addictive. The main difference is that we now understand receptors, including nicotinic acetylcholine and dopamine receptors, much better than we did in the past. We now see addiction, whether to smoking, cocaine, or sex through the lens of the neuronal receptor.

Is there evidence supporting the existence of pornography addiction? It depends on what one accepts, or can understand, as evidence, and this is a function of perspective and education. Perspective can introduce bias, and our perspectives are certainly multifaceted with regard to our attitudes. What may be meaningless to one may be definitive proof to another depending on differences in knowledge esoteric to the field in question. As T. S. Eliot said, "Where is the life we have lost in living? Where is the wisdom we have lost in knowledge? Where is the knowledge we have lost in information?" Given the current cultural climate with regard to sex, don’t hold your breath waiting for studies to come out showing that sexual activity should be restricted. Internet porn is the new drug, and as we found with alcohol, “prohibition” will not be tolerated by the fawning masses.

Yet it is my opinion, based on current addiction neuroscience, and the opinion of the American Society of Addiction Medicine (ASAM), that these individuals are either biased or uninformed, that there is overwhelming evidence that natural addictions exist, and that sexual addiction is real. Let us consider some of this evidence, looking back over the last decade. In 2001 Dr. Howard Shaffer, head of addiction research at Harvard said in the journal Science, “I had great difficulty with my own colleagues when I suggested that a lot of addiction is the result of experience ... repetitive, high-emotion, high-frequency experience. But it’s become clear that neuroadaptation—that is, changes in neural circuitry that help perpetuate the behavior—occurs even in

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10 T. S. Eliot, The Rock [1934],
the absence of drug-taking.”\(^{11}\) As Steven Grant at the National Institute for Drug Abuse (NIDA) said, "What is coming up fast as being the central core issue….is continued engagement in self destructive behavior despite adverse consequence."\(^{12}\)

In 2005 Dr. Eric Nestler, head of neuroscience at Mount Sinai and one of the world’s most respected addiction neurophysiologists published a landmark paper in Nature Neuroscience titled “Is there a common pathway for addiction?” in which he wrote, “Growing evidence indicates that the VTA-NAc pathway and the other limbic regions cited above similarly mediate, at least in part, the acute positive emotional effects of natural rewards, such as food, sex and social interactions. These same regions have also been implicated in the so-called ‘natural addictions’ (that is, compulsive consumption of natural rewards) such as pathological overeating, pathological gambling and sexual addictions.”\(^{13}\) Clearly the term addiction was moving from strictly behaviorally descriptive term to one that incorporated a biologic etiological component.

Based on continued research supporting a receptor model of addiction, in August of 2011 the American Society of Addiction Medicine released its new definition of addiction. Comprised of medical doctors, it is the organization representing the specialty of addiction medicine. Four years in the making and involving over 80 addiction experts, it made two clear and unequivocal statements. The first is that addiction is a chronic disease of the brain, affecting the reward, motivation, and memory systems. Second, addiction includes compulsive destructive behaviors involving sexuality, gambling, and overeating as much as substances such as cocaine and opiates. In other words, it’s not about the behavior or substance, it’s about the brain. With this definition it would seem the debate about whether or not sex can be an addiction would be over. To the medical specialty of addiction medicine, comprised of medical doctors who have an understanding and appreciation for

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12 Ibid
neurobiology and neuroscience, it is over, in the affirmative. Consider the following statement, for instance, from the definition:

“Addiction also affects neurotransmission and interactions between [memory] circuits and brain reward structures, such that the memory of previous exposures to rewards (such as food, sex, alcohol and other drugs) leads to a biological and behavioral response to external cues, in turn triggering craving and/or engagement in addictive behaviors.”

Dr. Michael Miller, representing ASAM said, "At its core, addiction isn't just a social problem, or a moral problem, or a criminal problem. It's a brain problem whose behaviors manifest in all these other areas... It's about underlying neurology, not outward actions." This understanding is important for many reasons. Take the concept of cross sensitization, for instance. An understanding that addiction to one drug or behavior can sensitize an individual to addiction to another drug or behavior based on pathologic reward pathway alterations common to any and all addictions. In 2001 Bradley and Meisel showed that sexual behavior sensitizes animals to amphetamine, and in 2003 Awena and Hoebel showed that sugar dependence sensitized animals to amphetamines as well. Dr. Eric Nestler cited cross-sensitization between drug addiction and natural addictions is one of the important evidences of the existence of these addictions. Cross-sensitization has a very important clinical implication in that therapists who don’t understand the neurologic aspects of how drug and natural addictions are intertwined will be at a disadvantage. ASAM’s Frequently Asked Questions site regarding its definition is important in explaining to the lay public why cross-sensitization matters: “We

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14 ASAM definition, long version
all have the brain reward circuitry that makes food and sex rewarding. In fact, this is a survival mechanism. In a healthy brain, these rewards have feedback mechanisms for satiety or ‘enough.’ In someone with addiction, the circuitry becomes dysfunctional such that the message to the individual becomes ‘more’, which leads to the pathological pursuit of rewards and/or relief through the use of substances and behaviors. So, anyone who has an addiction is vulnerable to food and sex addiction.”

Thus, mental health professionals who understand that food and sex addiction are a real with regard to the brain in terms of neuroplasticity will be better able to serve their patients and clients.

The American Psychological Association (APA) has been resistant to the addiction label for natural addictions in the past. The DSM manuals, which Congress has mandated are used to defined mental illness for insurance payment purposes and also by health care professionals have reflected this. Since the DSM is based on behavior rather than neurobiology, addictions are characterized separately based on the unique behavioral characteristics of each addiction, rather than seeing all addiction as a behavioral consequence of altered brain reward, motivation, and memory systems.

The problem is that the DSM is being made into something it was never intended to be, a definition of the biologic basis for addiction! Since 1980, for instance, the DSM has stated that its definitions of mental illness are “atheoretical;” in other words based on behavior as defined by observation and interview. The DSM has never claimed to be a textbook on the neuroscience of mental illness, so the current debate on whether to define obesity, sex, and gambling as addictive or merely compulsive in the coming DSM V is a behavioral debate, not one based on neurobiology. That some on the board formulating the pending DSM V might consider including obesity and gambling as addictive but not sex illustrates this “behavior rather than biology” conundrum. If online gambling is classified as a behavioral addiction in the DSM V, Internet pornography is online poker on

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steroids. It would defy logic to include poker and not porn! The payoff is masturbatory rather than monetary, but the reward circuits are the same. To call pathologic expression of sexuality “hypersexual syndrome” but not an actual addiction, yet to allow the addiction label to be applied to obesity and gambling is biologically inconsistent. Bottom line: the addiction label is no longer solely the APA and DSM’s call based on behavior; it now belongs also to ASAM and neuroscience based on biology. If I have a patient with a Grade IV astrocytoma who develops a severe depression, I will send him or her to a mental health professional for treatment, but I don’t expect that professional to understand the cause of the tumor or the nuances of combining surgery and radiation to treat it. It is not within the scope of the DSM to define the neurobiological basis of either astrocytomas or addictions; its focus is in the analysis, diagnosis, and treatment of the behavior. This controversy is one of perspective.

That many psychiatrists are embracing the addiction label with regard to sexual addiction is clear. For instance, Drs. Bostwick and Bucci at the Mayo Clinic recently published a case report describing treatment of Internet sex addiction with naltrexone, an opioid receptor antagonist. They summarized:

In summary, cellular adaptations in the addict’s PFC result in increased salience of drug-associated stimuli, decreased salience of non-drug stimuli, and decreased interest in pursuing goal-directed activities central to survival. In addition to naltrexone’s approval from the Food and Drug Administration for treating alcoholism, several published case reports have demonstrated its potential for treating pathologic gambling, self-injury, kleptomania, and compulsive sexual behavior. We believe this is the first description of its use to combat Internet sexual addiction.20

Dr. Nora Volkow is head of the National Institute on Drug Abuse (NIDA), and is one of the most published and respected addiction scientists in the world. She has recognized the change in the understanding of natural addiction in advocating changing the name of the NIDA to the National Institute on Diseases of Addiction, as quoted in the journal Science: “NIDA director Nora Volkow also

felt that her institute’s name should encompass *addictions such as pornography*, gambling, and food, says NIDA adviser Glen Hanson. ‘She would like to send the message that [we should] look at the whole field.’ (emphasis added)

Of course behavior is important, particularly as we learn of behavioral learning’s scaffolding and sculpting effect on the brain. Let’s take a few minutes and consider the brain.

At and in the head of the body, functionally and literally, is the brain. It is an intricate tapestry of 100 billion nerve cells, with at least another 100 billion or more supporting glial cells. Interestingly by comparison the Milky Way Galaxy is estimated to contain a comparable number of from 200 to 400 billion stars, with our sun being only a modest representative! When we consider the vast distances between individual stars in our galaxy it is difficult for us to understand any commonality of purpose. Yet when we look at our sister Andromeda galaxy we see the disc shape spiral, the rotation, the cohesion. Clearly the individual stars are connected through these cohesive forces, much as neurons in our brains communicate and compute.

A decade ago when a fellow physician called and asked if he could bring a CT of the brain by for me to review. It was his own brain. His group had purchased a new CT scanner, and he volunteered as the guinea pig to be the first to try it out. It showed, and an MRI confirmed, that he had a colloid cyst in his third ventricle, and it was already partially obstructing one of his lateral ventricles. I asked if he had a headache, and he said, “You know, I have had increasing headaches lately.” He begged me to let him fly out of town for the upcoming Final Four, to which he had tickets and at which his favorite team, Texas, was a participant. I described, in calculated detail, how colloid cyst could cause sudden death, and instead he was in surgery the next day where I removed the cyst. It required an interhemispheric approach, splitting corpus callosum and entering the lateral ventricle. After removing the cyst I could see the striatum, and by looking through the Foramen of Monroe could see into the third and visualize the hypothalamus. Because I know this person, who

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today continues to be a functioning physician, I experienced an epiphany of sorts. I realized that in these limbic structures his personality, his wants, desires, fears, and memory were imbedded. Through these delicate and sensitive neural instruments he was able to interface with the world. And I paused for a short moment of insight into who he was and who I am.

The exterior of our brain is covered by a carpet of neurons from our eyes to our occiput, the cerebral cortex. It is in the cortex that we see, think, judge, feel, move, taste, and live. Some areas of the cortex are strictly functional; if we are awake and see something, light reflecting off of the image strikes our retina and is carried to the occipital cortex where it is processed involuntarily as a photographic reproduction of the image carried by the light. Sounds are recorded and send by the inner ear to the auditory cortex where the noise is processed, and motor strip neurons initiate an electrical chain stimulating muscle cells to contract. Other cortical regions such as Weinike’s turn meaningless sounds into words and speech, and Broca’s cortex turn ideas and emotions into words. The cortex absorbs and processes information, but the limbic regions allow emotion and meaning to bring perspective to the information. For instance, the hippocampus is important in technical memory, while the amygdala records and processes emotional memory; it colors the black and white information with emotional Technicolor, to use a metaphor from Dr. Marc Lewis.  

Inherent in this limbic circuit are powerful reward pathways which motivate us to eat, to reproduce, to win. At the center of this system is the nucleus accumbens, with all roads leading to this Rome of the brain reward world, as Blum said. The neuronal cell bodies in the nucleus accumbens are coated with receptors to a variety of neurotransmitters, from glutamate and opioids to cannabinoids. Preeminent is this neurochemical potpourri are the dopamine receptors, ready to receive dopamine from across the synapse from dopaminergic pre-synaptic terminals at the end of axons originating in

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22 see Memoirs of an Addicted Brain by Dr. Marc Lewis, sections on psychedelics.
23 Blum et.al, The Addictive Brain: All Roads Lead to Dopamine. Journal of Psychoactive Drugs 2012
the ventral tegmental area of the midbrain, the dopamine pharmaceutical lab of the brain. We even call these pathways the dopaminergic reward systems in acknowledging this central role.

Dopamine is an excitatory catecholamine, differing only by a methyl group from its close cousin norephinepherine, seen on the bottom. These are true “brain drugs,” in that they are manufactured by both our brains and also by pharmaceutical labs to produce exactly the same effect. Dopamine is produced in the midbrain, in the ventral tegmental area (VTA). It powers the brain with desire, with motivation to do, to get, to receive the promised reward. It is important in our focusing on what we want, what we desire, rather than the resolution part of the reward, which is more the purpose of the natural opioids. These opioids provide the satiation, the euphoria of enjoying the reward. Dopamine focuses our attention of whatever reward we have taught our brain we most want with laser-guided intensity. This is good when we allow our frontal cortex to balance pleasure with judgment. Dopamine wants! Opioids like! They work in tandem, in a symphony of desire and reward, of craving and satiation. The memory of past rewards causes us to desire to experience the rewards again, and we boundary this desire with frontal control. The amygdala is the repository of these deep limbic memories, and it communicates with our frontal areas in providing meaning to the dopaminergic desire coming out of the VTA and to the satiation provided by opioids. The amygdala colors our pleasure with meaning, with purpose.

Our neocortex also projects to these limbic regions; it floods the nucleus accumbens and the dorsal striatum with glutamate, another excitatory neurotransmitter. These inputs carry different points of view, however. The orbitofrontal cortex (OFC) and dorsal anterior cingulate gyrus (dACG) both receive dopaminergic efferent input from the VTA also, and they appraise and judge the stimulus as they turn dopaminergic desire into a plan of action. Don’t just want it, do it! The OFC seems to be more important in stimulus selection. I want that one! It is the microscope that helps focus, with memory from the amygdala, on a particular craving, a specific addiction, while the dACG helps with the plan on action.
Our OFC, ACG and associated frontal control centers ride above, physically and functionally, on the wild horse of the amygdala, the VTA, the NA, and the other desire-driving limbic regions. These frontal regions provide a bridle, a brake, to keep this horse in check.

When we allow the limbic horse to run unbridled, several physical and neurochemical changes occur in the brain, and a state of addiction ensues. First, overutilization of the dopaminergic pathways facilitates a downgrading of the system, which resets the hedonistic set point. This creates a new normal, a ‘dopamine dearth’ of sorts, which motivates the individual to act out in addiction in an attempt to return to homeostasis. Of course, addiction is anything but homeostasis, and repeated binges simply worsen the imbalance. The downgrading occurs in the nucleus accumbens, where less dopamine is produced by progressively atretic VTA cells, and there is less dopamine available in the pre-synaptic vesicles as well. There is also a downgrading of receptors on the post synaptic terminals of the medium spiny neurons in the NA. We see this downgrading when we label dopamine receptors with markers such as Raclopride, and we can see decreased metabolism in reward structures in response to a stimulus challenge in both drug and in natural addiction as well.

Decreased receptors have been seen not only in drug addiction, but also in obesity. Decreases in metabolic function has been seen in drug addictions and in both obesity and gambling. That these changes are causative is clear. For instance, we see recovery of dopaminergic receptor function with weight loss after gastric banding surgery.

Second, these metabolic changes are seen both chemically and micro-structurally. Consider DeltaFosB, a protein found a decade ago to be chronically elevated specifically in the medium spiny

26 Kimberley E. Steele, Gregory P. Prokopowicz, Michael A. Schweitzer, Thomas H. Magunsmuon, Anne O. Lidor, Hiroto Kuwabawa, Anil Kumar, James Brasic and Dean F. Wong Alterations of Central Dopamine Receptors Before and After Gastric Bypass Obesity Surgery Volume 20, Number 3, 369-374, DOI: 10.1007/s11695-009-0015-4
neurons of the nucleus accumbens in the brains of drug addicted laboratory animals. Subsequent studies have shown it to be elevated in these same cells in animals manifesting pathologic overconsumption of natural rewards such as to food and sex.\textsuperscript{27} It now appears that DeltaFosB is a molecular transcription switch which turns on other gene sets which then mediate neuroplastic change in these neurons; in other words they promote neural learning. We know it has a physiologic role in sex; it is the level that is important; in supra-physiologic amounts it causes overconsumption. We use the term neuroplasticity to denote physical changes that occur in neurons with learning. As Malenka and Kaeur said in their paper on synaptic plasticity: “Addiction represents a pathological but powerful form of learning and memory.” Addiction is learning on a neuronal basis to crave rewards that not only don’t enhance survival, but are harmful. It is cellular learning gone dreadfully wrong. Pornography viewing is an exercise in neuronal plasticity and leaning, with the frantic searching and evaluating each clip of video for the promise of maximal masturbatory sexual reward.

Supraphysiologic levels of DeltaFosB appear to portend addiction, as described by Dr. Eric Nestler in his Royal Society paper on the role of DeltaFosB in both drug and natural addiction: “The nucleus accumbens is believed to function normally by regulating responses to natural rewards, such as food, drink, sex and social interactions. As a result, there is considerable interest in a possible role of this brain region in so-called natural addictions...we and others have found that high levels of consumption of several types of natural rewards leads to the accumulation of \( \Delta FosB \) in (the) nucleus accumbens. This has been seen after high levels of wheel running as well as after chronic consumption of sucrose, high-fat food or sex. These findings suggest that \( \Delta FosB \) in this brain region sensitizes animals not only for drug rewards but for natural rewards as well, and may contribute to states of natural addiction.”\textsuperscript{28}

He continues:


“...it raises the interesting possibility that levels of DeltaFosB in nucleus accumbens or perhaps other brain regions could be used as a biomarker to assess the state of activation of an individual's reward circuitry, as well as the degree to which an individual is ‘addicted,’ both during the development of an addiction and its gradual waning during extended withdrawal or treatment.”

Subsequent DeltaFosB studies have strengthened the concept of natural addiction, such as the Wallace paper, which examined the role of DeltaFosB in overconsumption of two natural rewards, food and sex: “In summary, the work presented here provides evidence that, in addition to drugs of abuse, natural rewards induce ΔFosB levels in the NAc...our results raise the possibility that ΔFosB induction in the NAc may mediate not only key aspects of drug addiction, but also aspects of so-called natural addictions involving compulsive consumption of natural rewards.”

Whereas maintaining a certain physiologic level of reward incentive advantageous to the survival of the organism and species may be a role of DeltaFosB, overexpression is associated with pathologic overconsumption and thus can be an indicator of addiction. This causative role for DeltaFosB in overconsumption has been demonstrated. Two mechanism have been used to genetically manipulate DeltaFosB independent of behavioral variables. One involves producing lines of bitransgenic mice which selectively over-produce DeltaFosB specifically in the striatal reward areas. These genetically altered animals thus phenotypically exhibit addictive overconsumptive behavior. The second involves transfer of genes through adeno-associated viral vectors into adult animals which then induce over or under expression of DeltaFosB. For instance, when overexpression of DeltaFosB was imposed through these viral vectors in laboratory animals, they exhibited a supraphysiologic enhancement of sexual performance. Conversely, repression of DeltaFosB

29 Ibid.
31 Ibid
decreases performance, thus confirming a role in normal physiologic homeostasis. As Nestler stated in the Royal Society paper, the important thing is the degree of DeltaFosB induction, with overexpression corresponding to overconsumption and addiction. DeltaFosB has been shown to be a mediator in protecting against depression-inducing stress as well, and induction of DeltaFosB has been shown to be required for fluoxetine (Prozac) to exert its anti-depressive effects. Depression and addiction often go together however; this complex relationship is explained in this commentary from the National Institute of Mental Health on this paper: “Depressed patients often lack motivation and the ability to experience reward or pleasure — and depression and addiction often go together.

Indeed, mice susceptible to the depression-like syndrome show enhanced responses to drugs of abuse, the researchers have found.

But the similarity ends there. For, while an uptick in DeltaFosB promotes addiction, the researchers (Nester et. al.) have determined that it also protects against depression-inducing stress. It turns out that stress triggers the transcription factor in a different mix of nucleus accumbens cell types — working through different receptor types — than do drugs and natural rewards, likely accounting for the opposite effects.”

DeltaFosB is a molecular switch, a transcription product that turns on other genes which initiate cascades important in neuroplasticity in many areas of the brain. For instance, DeltaFosB increases dendritic spine density in medium spiny neurons in the NA in addicted animals during extended periods of abstinence through stimulation of the protein Cdk5, thus becoming a bridge to more

extended neuroplasticity.\textsuperscript{36} Other proteins such as Brain Derived Neurotrophic Factor (BDNF) accumulate during abstinence, and may be important in driving relapse in cocaine addiction.\textsuperscript{37} Powerful craving states associated with addiction produce these morphologic changes in reward system neurons. These changes include dendritic arborization, and somal hypertrophy and atresia, as demonstrated in this illustration from Dr. Eric Nestler’s landmark paper published in Nature Neuroscience, “Is there a common pathway for addiction?” \textsuperscript{38} Significantly, sexual activity has been found to produce dendritic arborization as well.\textsuperscript{39} That sex can produce neuroplastic cellular changes identical to drug addiction is telling, both from the survival/incentive and the addiction perspectives. These switches are involved in producing visible neuroplastic change in neuronal populations specific to incentive pathways. Nature thus ensures that we will seek activities that support our survival, such as eating and sex. Salt is essential to our survival, and there is an interesting correlation with addiction and salt. Salt depletion causes a strong craving in animals so depleted, and this is also associated with similar dendritic changes in nerve cells to those already discussed with sex\textsuperscript{40} and drugs.\textsuperscript{41} That salt and sex craving both are associated with neuroplastic change is not


surprising from a survival standpoint; both are essential in this regard. We have mentioned that
dendritic sprouting has been seen in these neuronal populations in drug rewards such as cocaine or
amphetamine, and in natural rewards such as sex. Salt depletion, like sex, has cross-
sensitization effects to drugs as well. This is not surprising in light of a recent paper published last year in the Journal of the Proceedings of the National Academy of Sciences (PNAS) in which I was a co-author titled “Relation of addiction genes to hypothalamic gene changes subserving genesis and
gratification of a classic instinct, sodium appetite.” We found that sodium depletion kindled
expression of genes in the hypothalamus important in reward and neuroplasticity. Importantly, we
found that blocking dopamine receptors decreased gratification by depressing reward incentive.
Using gene set enrichment analysis we found that these same gene sets, that is the ones mobilized
by salt craving, are the same gene sets previously linked to cocaine and opioids. Of course, salt
craving has of necessity phylogenetically conserved across all in biologic systems, whereas drug
craving is the newcomer. As worded in our paper, “Drugs causing pleasure and addiction are
comparatively recent and likely reflect usurping of … ancient systems with high survival value by the

41 Roitman MF, Na E, Anderson G, Jones TA, Berstein IL. Induction of a Salt Appetite Alters Dendritic
Morphology in Nucleus Accumbens and Sensitizes Rats to Amphetamine. The Journal of Neuroscience 2002
42 Robinson TE, Kolb B. Alterations in the morphology of dendrites and dendritic spines in the nucleus
accumbens and prefrontal cortex following repeated treatment with amphetamine of cocaine. European Journal
of Neuroscience 11:1598-1604.
43 Pitchers, K.K.; Balfour, M.E.; Lehman, M.N.; Richtand, N.M.; Yu, L.; Coolen, L.M. Neuroplasticity in the
mesolimbic system induced by natural reward and subsequent reward abstinence. Biol. Psychiatry 2010, 67,
872-879.

44 Bradley KC, Meisel RL. Sexual Behavior Induction of c-Fos in the Nucleus Accumbens and Amphetamine-
45 Roitman MF, Na E, Anderson G, Jones TA, Berstein IL. Induction of a Salt Appetite Alters Dendritic
Morphology in Nucleus Accumbens and Sensitizes Rats to Amphetamine. The Journal of Neuroscience 2002
Lawrence AJ, and Denton DA. Relation of addiction genes to hypothalamic gene changes subserving genesis
and gratification of a classic instinct, sodium appetite. Proceedings of the National Academy of Sciences
gratification of contemporary hedonic indulgences.”\textsuperscript{47} National Geographic described our paper as follows: “Cocaine Addiction Uses Same Brain Paths as Salt Craving,” saying “Drugs hijack instinctual need for salt.”\textsuperscript{48}

I think our word “usurp” and their word “hijack” are accurate and descriptive with regard to what happens in addiction. These powerful survival cravings ensure that we will seek out these rewards or we will perish as individual organisms and as a species. Drug addiction usurps and hijacks these pathways and lies to the brain, telling the organism that it will die, it will perish, it if does not satiate the craving. Hence the difficulty with overcoming addiction though willpower alone, and the fallacy of trying to understand all addiction behaviorally without understanding or considering biology!

Can behavior change the brain macroscopically? Of course! As Zatorre and colleagues said in their Nature Neuroscience paper on neuroplasticity: “The brain is the source of behavior, but in turn it is modified by the behaviors it produces…”

...learning sculpts brain structure.”\textsuperscript{49} That DeltaFosB mediated neuronal dendritic scaffolding precedes macroscopic gyral sculpting has become clear.

In 1995 the Elbert study published in \textit{Science} demonstrated that increased use of the left hand in string players increased the corresponding cortical grey matter representing the fingers of the players, and this causative enlargement was dependent on the age at which the musician began studying.\textsuperscript{50} Draganski’s paper in \textit{Nature} describes how structural changes in grey matter are induced by training,\textsuperscript{51} and Draganski and May summarized in Behavioral Brain Research in 2008: ““Contrary to

\textsuperscript{47} Ibid.
\textsuperscript{49} Zatorre et.al., Plasticity in gray and white: neuroimaging changes in brain structure during learning. \textit{Nature Neuroscience} 15, 528-536, 2012
assumptions that changes in brain networks are possible only during critical periods of development, modern neuroscience adopts the idea of a permanently plastic brain.⁵² The Schwenkreis study in 2007 demonstrated representative enlargement of the motor cortex associated with the left hand in violin players as compared to controls in support of the Elbert paper, and these authors summarized that “cortical asymmetries are the result of use-dependent plasticity as a specific consequence of extensive musical practice.”⁵³

Other studies reveal this cortical plasticity with use or disuse.⁵⁴ Draganski and associates paper demonstrating increase in gray matter in medical students after a three month period of intense studying in the hippocampi and in the parietal lobes.⁵⁶ The premise that the brain changes both micro and macroscopically with learning is accepted by those esoteric to the field of neuroscience with little debate. Learning changes the brain, and we can image this structurally. Consider the following statements representative of current concepts regarding neuroplasticity. From the Journal of Neuroscience: “Recent cross-sectional voxel-based morphometry (VBM) studies have demonstrated learning-dependent changes in the adult human brain and suggested anatomical correlates for navigation, arithmetic, linguistic, procedural, and musical learning abilities.” (Maguire et al., 2000; Golestani et al., 2002; Sluming et al., 2002; Gaser and Schlaug, 2003; Draganski et al., 2004).⁵⁷ From Behavior Brain Research: “Contrary to assumptions that changes in brain networks are possible only during critical periods of development, modern neuroscience adopts the idea of a permanently

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⁵² Draganski and May, *Behavioral Brain Research* 2008


⁵⁷ Ibid
plastic brain.” From Nature Neuroscience: “Human brain imaging has identified structural changes in gray and white matter that occur with learning...Greater dialog between researchers in these different fields would help to facilitate cross-talk between cellular and systems level explanations of how learning sculpts brain structure.” Remember Kauer and Malenka’s comment in their paper on synaptic plasticity and addiction, that “addiction represents a pathologic but powerful form of learning and memory?” We should not be surprised then to learn that addiction studies show cortical atresia macroscopically. Virtually every study on addiction has demonstrated atrophy of multiple areas of the brain, particularly those associated with frontal control and the reward centers. This is true for drug addictions such as to cocaine, methamphetamine, and opioids, but also in behavioral conditions associated with pathologic overconsumption of natural rewards and behaviors such as food, sex, and Internet addiction. Of course, these were correlative studies, and critics will point to the inevitable warts inherent in any correlative study. But in doing so they ignore the


forest of prospective work on addiction and the cortical plasticity learning studies we have cited. Consider, for instance, this statement from the Draganski paper published in Nature in 2004 “Does the structure of an adult human brain alter in response to environmental demands? Here we use whole-brain magnetic-resonance imaging to visualize learning-induced plasticity in the brains of volunteers who have learned to juggle. We find that these individuals show a transient and selective structural change in brain areas that are associated with the processing and storage of complex visual motion. This discovery of a stimulus-dependent alteration in the brain's macroscopic structure contradicts the traditionally held view that cortical plasticity is associated with functional rather than anatomical changes.” Positive neuroplasticity has been demonstrated as in the study on methamphetamine addiction which demonstrated a return to more normal cortical volumes with recovery from addiction, or the VBM study by Holzel et.al. on enlargement of gray matter after mindfulness therapy is an example of positive macroscopic plasticity. The authors summarize, “The adult nervous system has the capacity for plasticity, and the structure of the brain can change in response to training.” These studies also support causation. Regarding pornography and plasticity Dr. Norman Doidge, a Columbia psychiatrist, said, “The addictiveness of Internet pornography is not a metaphor. Not all addictions are to drugs or alcohol. People can be seriously addicted to gambling, even to running. All addicts show a loss of control of the activity, develop tolerance so that they need higher and higher levels of stimulation for satisfaction, and experience withdrawal if they can’t consummate the addictive act. All addiction involves long-term, sometimes lifelong, neuroplastic change in the brain.”

An important component of ASAM’s new addiction definition is the issue of hypofrontality, or impairment of executive function. This results in an inability to correctly weight the consequences of

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68 Holzel et. al., Mindfulness practice leads to increase in regional brain gray matter density. *Psychiatry Research: Neuroimaging* 2011

69 Norman Doidge, MD *The Brain That Changes Itself*, pg 106.
using drugs or engaging in behaviors pathologically as the OFC and cACG become impaired. The ‘brake pads’ of the brain wear out. Fowler, Volkow, Kassed and Chang described an interesting parallel in a paper concerning frontal impairment in addiction: “…studies have shown that cocaine and methamphetamine reduce cellular activity in the orbitofrontal cortex, an area we rely on to make strategic, rather than impulsive, decisions. Patients with traumatic brain injuries to this area of the brain display problems – aggressiveness, poor judgment of future consequences, inability to inhibit inappropriate responses – that are similar to those observed in substance abusers.”

As a neurosurgeon who has treated patients with frontal lobe impairment as a result of trauma, tumor, stroke, or bleeding I agree that they can manifest this constellation of behaviors. Does this mean that because all individuals with drug or behavioral addictions will exhibit executive control deficits in all areas? Of course not. In the late 1800s the miracle of local anesthetic blocks were discovered in the effects of cocaine. Cocaine solution in the eye revolutionized painful cataract surgery overnight. William Halstead, a talented young surgeon found that it was useful as an anesthetic local block. Unfortunately, he and many other physicians found that this useful and harmless, they thought, white powder also provided quite a punch recreationally. William Halstead became addicted to cocaine, and the treatment then was to use morphine to smooth out the cocaine. He went on to revolutionize the field of surgery, becoming the chief of surgery at the new Johns Hopkins Medical School. His principles of surgical technique are well know and used by surgeons even today, yet it is now well documented through the Osler papers that he struggled with addiction to both of these drugs. I am personally grateful to him for his work because the neurosurgeon who trained me, Dr. James T. Roberson, was trained by Dr. Semmes and Murphey, both of whom were exposed to and received training from Dr Harvey Cushing, the father of neurosurgery in this country and who himself was

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70 Fowler JS, Volkow ND, Kassed CA, Chang L. Imaging the Addicted Human Brain. *Science and Practice Perspectives* 3(2) April 2007, 4-16.
trained by Dr. Halstead. It is remarkable that Dr. Halstead was able to function at such a high level of executive function despite with serious drug addiction.

Before he gained his PhD and became a well-published neuroscientist, Dr. Marc Lewis experienced addiction to virtually every drug imaginable. He wrote of his experiences in a book, “Memoirs of an Addicted Brain.” He describes what the drug trips of the various drugs were like, and details how the cravings that led him to relapse over and over felt. He then explains the neuroscience behind the sensations and cravings. He said, “dopamine-powered desperation can change the brain forever, because its message of intense wanting narrows the field of synaptic change, focusing it like a powerful microscope on one particular reward. Whether in the service of food or heroin, love or gambling, dopamine forms a rut, a line of footprints in the neural flesh. And those footprints harden and become indelible, beating an intractable path to a highly specialized – and limited – pot of gold.”

These dopaminergic ruts in the neural flesh thus are harbingers of the scaffolding and sculpting which are characteristics of pathologic, yet powerful learning, as Kauer and Malenka said, whether the ruts are cut as a result of substance or behavioral addictions. That the cost of natural addictions rivals and even surpasses drug additions should not surprise us if we understand the receptor model of addiction. Considering, for instance, the social cost of substance addictions and just one natural addiction, obesity, the natural addiction eclipses substance addictions by 10 billion dollars a year. Add the cost lost productivity in the workplace and job terminations from Internet pornography in the workplace and the number balloons.

The demographic, human cost is, I believe, much higher with regard to pornography addiction. Dr. Philip Zimbardo describes the current “demise of guys,” as he calls it, as primarily due to “arousal addiction,” and says it is distracting men from success. He believes it is primarily due to excessive new access to pornography and video games. He says, “Boys brains are being digitally rewired in a new way for change, novelty, excitement and constant arousal; that means they are totally out of sync

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72 Marc Lewis, Memoirs of an Addicted Brain; A Neuroscientist Examines His Former Life on Drugs. Public Affairs, New York. 2011 pg 156.
in traditional classes which are analog, static, interactively passive…and in romantic relationships, which build gradually and subtly.” 73 I agree with Dr. Zimbardo, and believe pornography is inducing a cultural pheromonic effect. In 1869 the gypsy moth was brought to America to attempt to jump start a silk industry. Rarely have good intentions gone so wrong, as the unforeseen appetite of the moth for deciduous trees such as oaks, maples, and elms has devastated forests for the last 150 years. Numerous strategies have been employed to destroy this pest. However, in the 60’s scientists noted that the gypsy moth male finds the female to mate with her by following her scent. This scent is called a pheromone, and is extremely attractive to the male. In 1967 a paper was published in the journal *Nature* which used pheromones to prevent the moths from mating. The scientists mass-produced the pheromone and permeated the moth’s environment with it. This unnaturally strong scent overpowered the normal females ability to attract the male, and the confused males were unable to find the females. Note the title of the paper, “Insect population control by the use of sex pheromones to inhibit orientation between the sexes.” 74 Also pertinent is this summary from the abstract of the paper: “We have for the first time obtained experimental confirmation that pre-mating communication between the sexes can be disrupted by permeating the atmosphere with an insect pheromone.” 75 A follow up paper in 1972 describes population control of the moths by “preventing male gypsy moths from finding mates.” 76 The gypsy moth was the first insect to be controlled by the use of pheromones, which work by two methods. One is called the confusion method. An airplane scatters an environmentally insignificant number of very small plastic pellets imbedded with the scent of the pheromone, and only a few of these pellets per acre are enough to overpower the male’s ability to find the female. He is thus desensitized to the natural scent of the female by this artificially

73 Philip Zimbardo, The Demise of Guys, [http://www.youtube.com/watch?v=FMJgZ4s2E3w](http://www.youtube.com/watch?v=FMJgZ4s2E3w) see also ebook on Kindle, same name.
75 Ibid
produced pheromone. An Australian article describes the confusion method as follows, “The male either becomes confused and doesn’t know which direction to turn for the female, or he becomes desensitized to the lower levels of pheromones naturally given out by the female and has no incentive to mate with her.”

The other method is called the trapping method, in which the male moths enter traps from which they cannot exit looking for the female, only to find a fatal substitute.

Pornography is a visual pheromone, a powerful 100 billion dollar per year brain drug that is changing sexuality even more rapidly through the cyber-acceleration of the Internet. It is “inhibiting orientation” and “disrupting pre-mating communication between the sexes by permeating the atmosphere” and Internet.

It was Dr. Kenneth Blum who coined the term “reward deficiency syndrome” to frame a neurologic basis for natural addiction years ago based on a dopamine receptor model. He said, “The conviction that drug and alcohol dependence was a disease rather than a symptom of moral weakness was growing in the late nineteenth and early twentieth century, there was no knowledge of how the disease might be acquired or treated. Importantly, the therapies used to treat this disease remained focused solely on psychological factors and lifestyle behavior modification (with the help of drugs) as if it were still a psychiatric condition rooted in moral weakness. The good news today is that under-standing that low dopamine function leads to impulsive, compulsive and addictive behaviors paves the way to defining addiction as a brain disorder involving impairments in so-called “reward circuitry” (Blum et al. 2000). This definition of addiction has now been adopted by the American Society of Addiction Medicine (ASAM 2011), which was founded by the San Franciscan visionary David E. Smith (Sturges 1993)… An orgasm is the primary natural blast of dopamine available to all of us. Accordingly, J.R. Georgiadis (2006) scanned the brains of people having orgasm. He said they

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resembled scans of heroin rushes. These individuals experienced one of the most addictive substances ever produced: dopamine.\textsuperscript{79}

Back to the first medical use of the word addiction in the Journal of the American Medical Association in 1906 in the context of opium addiction, “It matters little whether one speaks of the opium or sexual habit, the opium or sexual disease, or the opium or sexual addiction.”\textsuperscript{80} Armed with an understanding of the neuronal receptor we can just as easily substitute the word sexuality for opium. Yes, words are important, sex can become a brain modulating disease, the disease of addiction. It is critical for professionals treating sexual addiction to understand and teach this, for, as Dr. John Mark Haney said: “Since pornography can be an addiction, \textit{these “just say no” types of approaches are likely to only create more frustration and self-defeating ideation... the intervention and treatment modality must recognize the problem as a full addiction, and treat it with the same consideration given to alcohol or chemical substances.}”\textsuperscript{81}

The term hypersexual rather than addiction is accurate and consistent only if we use terms such as hyperphagia, hypergambling, hypercocaine, and hyperheroin syndrome.

We need to continue to learn all we can about the behavioral aspects of addiction, but we must understand that when the DSM I came out in 1952 the concept of the receptor model of addiction was years in the future. This was still true when the DSM III admitted and stated that its definitions of mental illness were ‘atheoretical,’ that is, not based on etiology or attempting to explain causation biologically. However, now that we are not as neurologically naïve, it is incumbent upon those responsible for formulating the DSM V and future editions not to continue to reflect this naivety. To recognize gambling as a behavioral addiction, but not food or sex is not only confusing, especially to the uninformed, it is inaccurate and inconsistent based on current neuroscience. It only fuels...

\textsuperscript{79} Blum, et. al, The Addictive Brain: All Roads Lead to Dopamine. \textit{Journal of Psychoactive Drugs} 2012

\textsuperscript{80} JAMA, March 3, 642/2, 1906

concerns about the objectivity of the DSM, and unfortunately will serve to decrease its credibility and influence, especially in the eyes of scientists who understand what a neuronal receptor is. This issue is much like the issue and controversy surrounding childbed fever in the 1800s. The germ theory of disease had not yet been formulated. Doctors in delivery wards would check the service of women in labor, and would not wash their hand between patients. They had no explanation for the high death rates in these young mothers; they would become febrile and die within one to two weeks. Ignaz Semmelweis, a young Hungarian physician training in Vienna noted that a fellow physician died of the same symptoms after cutting his hand with a scalpel with had been used on the women. He made the correlation between the matter on the knife and the death of his friend. He began to wash his hands between patients, and noted in 1847 that this febrile illness was eliminated. Throughout his career, despite his patients enjoying protection from childbed fever, the prevailing dogma in the large medical centers was that the disease was miasmic in etiology, or from bad air. He was opposed at every turn by the medical establishment, who continued to wipe their hands on their coats and infect their patients. It wasn’t until years after his death, after Joseph Lister and Robert Koch, that he was vindicated. This amazing disconnect has made it into the lexicon and is called the Semmelweis reflex or effect. It is defined as the tendency or even reflex to reject new evidence that contradicts an established paradigm. The evidence is clear for ASAM and others versed in receptor-based behavioral neuroscience; indeed the paradigm has shifted with regard to addiction. It may be the VI, VII, or X before the DSM gets it right, but SASH conferences at some point in the future will look back at this discussion with the same amazement that we look at those who questioned Semmelweis. Of course we need behavioral research into sexual addiction, but we must also consider that sexual behavior is woven into affecting, and affected by the biology. As Lewis, Amini, and Lannon said, But
dividing the mind into ‘biological’ and ‘psychological’ is as fallacious as classifying light as a particle or a wave.” In perhaps no other human function is this concept better illustrated than in sexuality.

With regard to recovery, let’s consult Shakespeare through Hamlet, “Refrain tonight, and that shall lend a hand of easiness to the next abstinence; the next more easy; for use almost can change the stamp of nature…”

There is indeed a stamp, a rut, in the brain, imposed by addiction. Recovery requires that same neuroplastic process. Thank you for your work to change the stamp of nature as your clients seek to heal and recovery sexually and find fulfillment in their lives, and I thank you for your attention today.

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83 William Shakespeare, Hamlet, Act 3, Scene 4