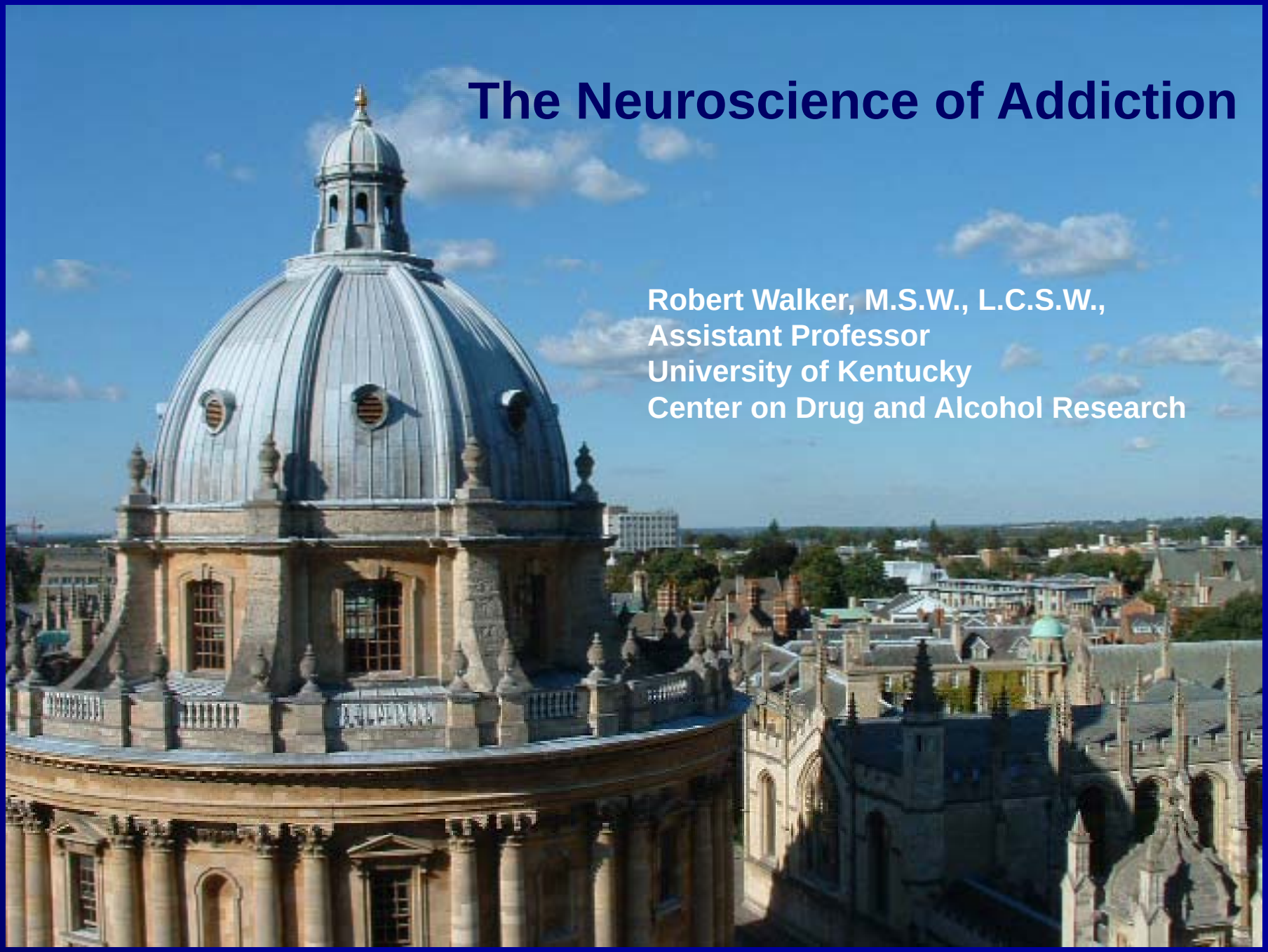
The Neuroscience of Addiction



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Why do we need the science on addiction for community projects?

- First, there is a growing body of neuroscience about the brain as well as social and psychological research about behavior.
- Much of the research challenges our daily attitudes and beliefs about addiction.
- Second, with a new special project, it can be useful to try and draw people together into a more closely shared perception of the problem to be addressed.

The Beginning Point

- Neuroscience, over the past 50 years has shown that every thought, sensation, emotion, physical movement is accounted for in terms of brain structures and chemistry.
- This is not say that everything is *caused* by neurons, but nothing happens in human behavior except by the mechanisms of the brain.
- Behavior, including addiction is related to:
  1. Anatomical characteristics of brain regions;
  2. The functions of neurons, including their connectivity into pathways or “circuits”; and,
  3. The neurochemistry that exists between neurons that allows them to interact.

Brain and Behavior: The 2-Way Street

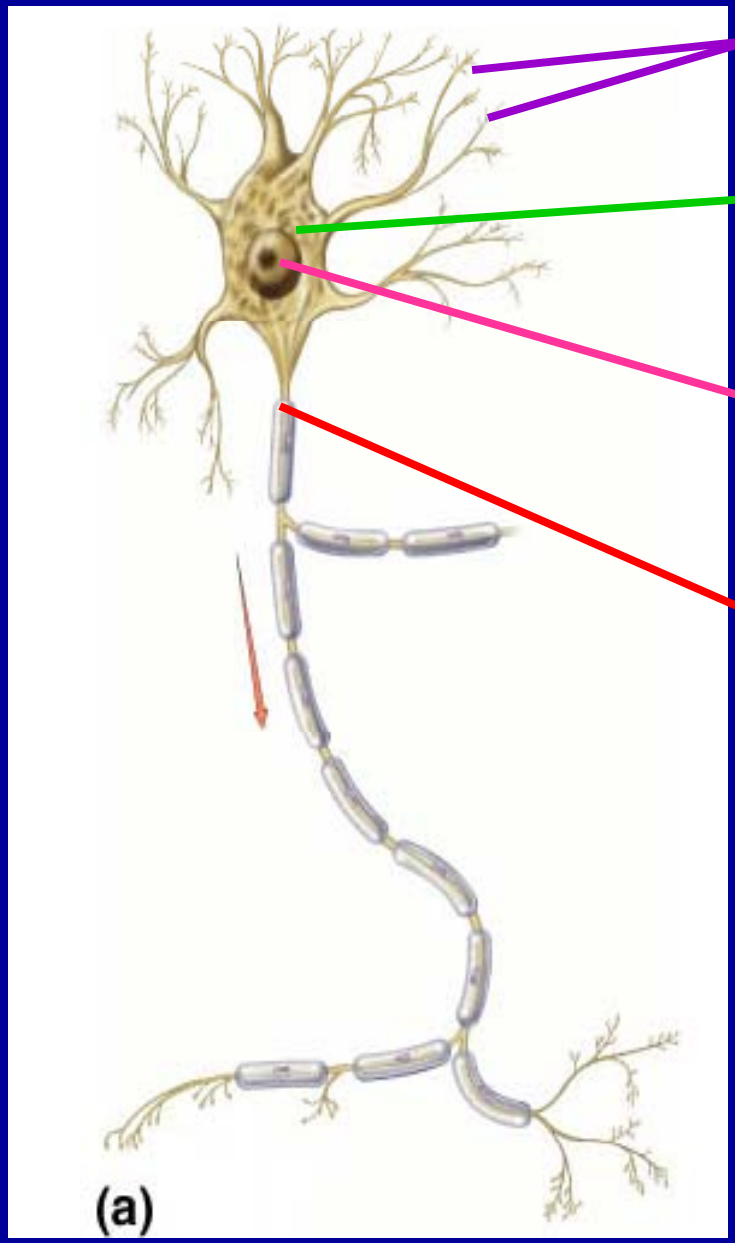
- Thinking, feeling and behaving *are* *produced* by brain anatomy and chemistry.
- However, thinking, feeling and behaving *shapes* the development of brain anatomy and chemistry.
- Just as brain structures can affect behavior (e.g., a stroke's effect on speech), likewise personal experience can affect brain structures.
- For example, the experience of severe trauma, severe chronic depression, or long term abuse of alcohol, have all been shown to result in loss of brain cells in the brain's memory-forming and retrieving center, the hippocampus.

The neuron

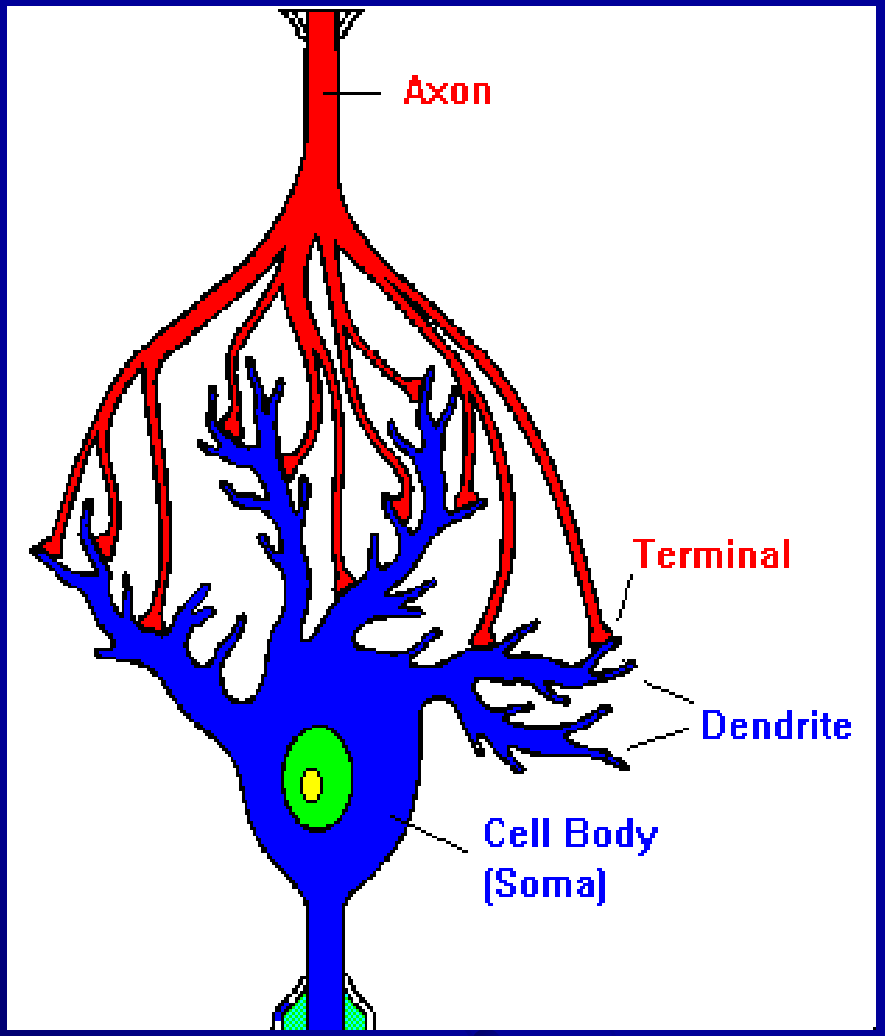
The cell body has a nucleus and numerous organelles

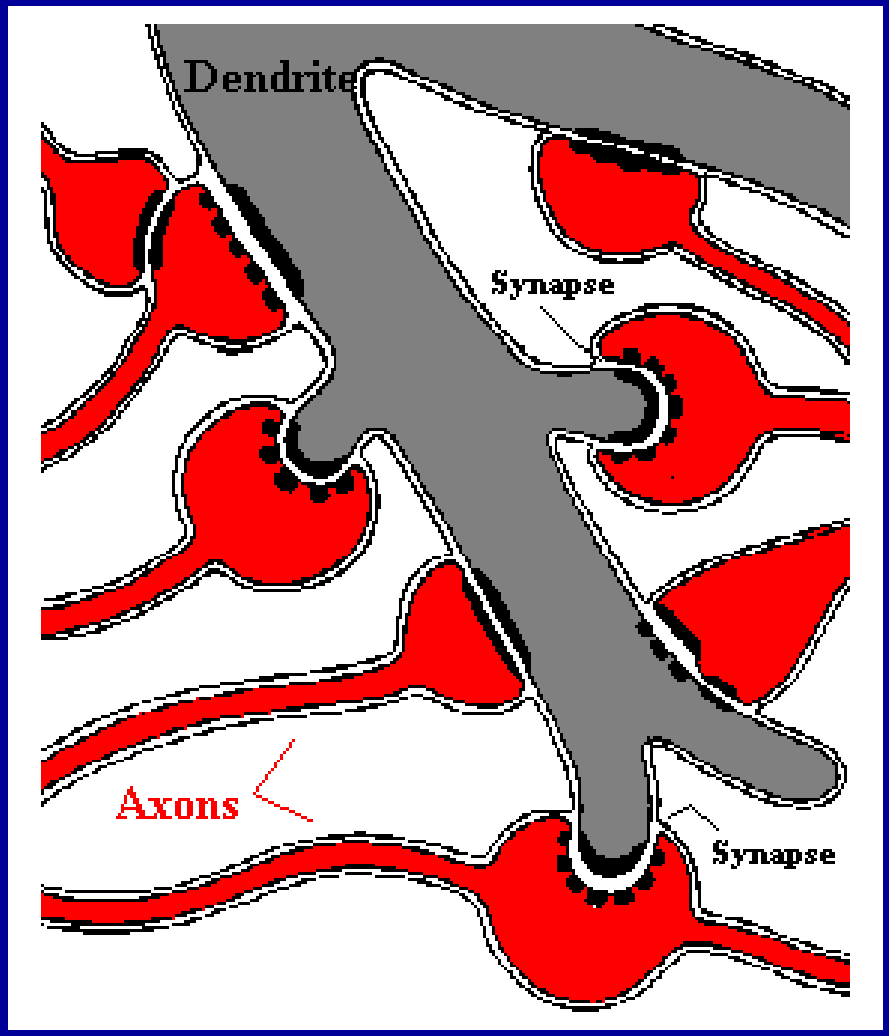
A single axon carrying impulses **away** from the cell body

One or more dendrites bringing impulses **in** to the cell body



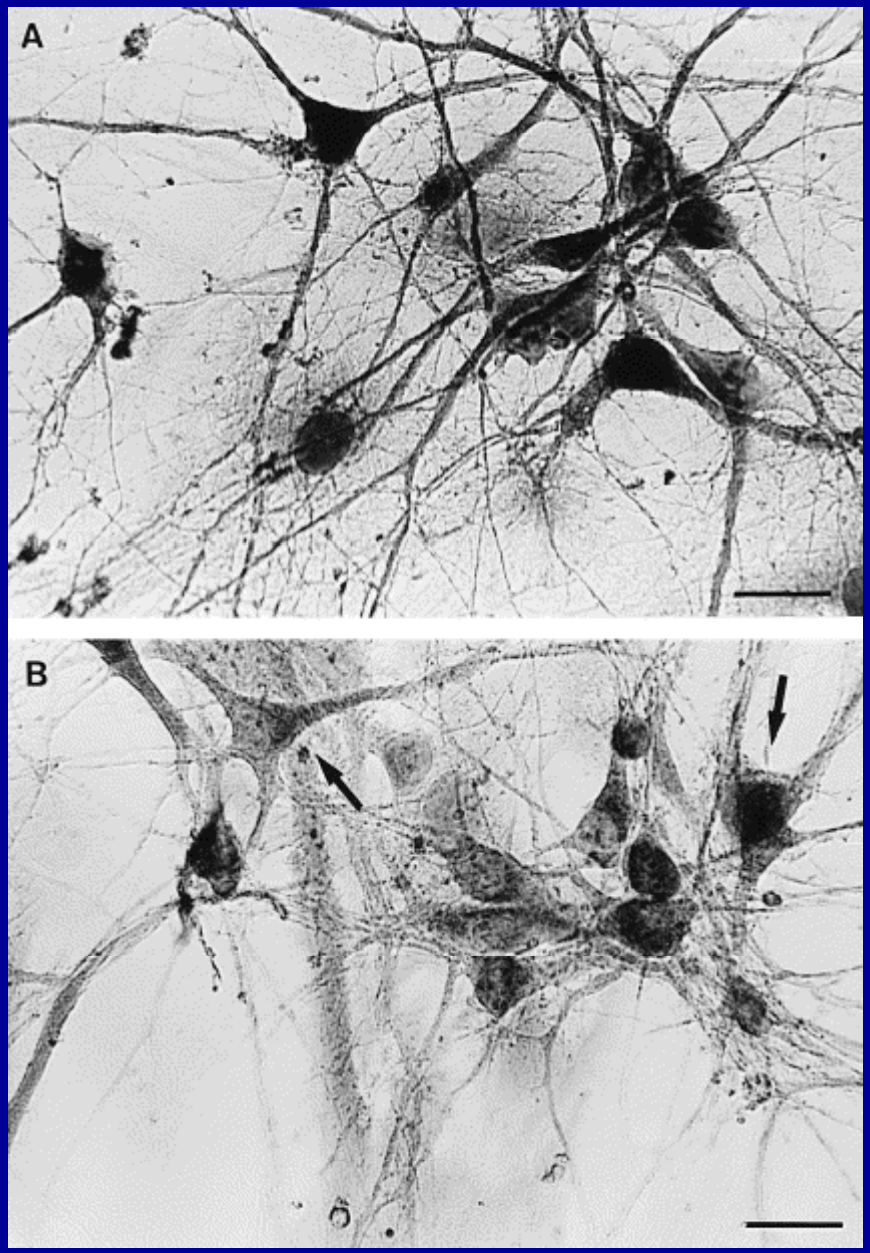
Neurons, receptors





http://faculty.washington.edu/chudler/synapse.html

What they actually look like



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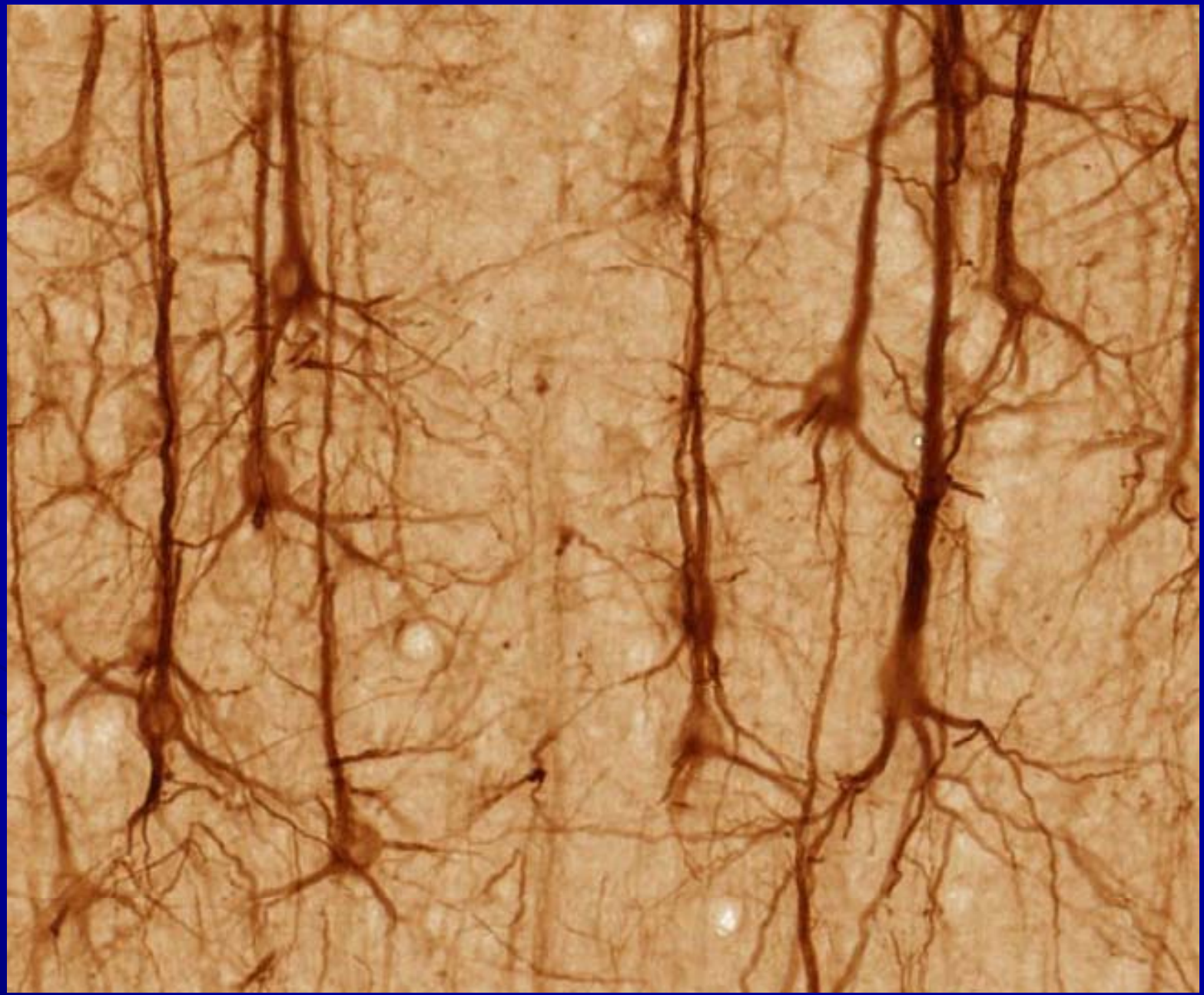


Much is known – more is unknown

- There is scientific data on about 50 neurotransmitters (the chemicals that create nerve cell communication) and there are probably some 300 neurotransmitters in the human brain.
- Recent technology allows very fine-grained detail not only about core structures in the brain but also what regions are activated during specific tasks or experiences.
- So, for example, imaging a brain while the person is watching a film shows that the occipital lobes are greatly activated because this is where visual information is first processed in the primate brain.
- Naturally, this kind of regional diversity leads to the question “What parts of the human brain are involved in addiction?”

The Science of Addiction

- There is a growing body of evidence of structural vulnerability of brains to the effects of intoxicating substances.
- Several factors contribute to this vulnerability:
  1. Genetic
  2. Early developmental influences and environmental factors
  3. Effects of stressful life events across the life cycle
  4. Mental disorders – principally depression and anxiety

Who is vulnerable?

- Persons most at risk for substance abuse and more so, dependence, generally have higher rates of impulsivity, more difficulty managing negative affects – their moods and feelings.
- It might be said this way: There is a lack of a balancing mechanism in some brains and this can affect a person's thinking, behaving, and range of emotions.
- The drug dependent person, even before ever using drugs, has brain characteristics that may predispose a vulnerability to the effects of mind-altering drugs.
- After a long period of using drugs, the addicted person ends up with a substantially altered brain – chemically and even anatomically.

What drives addiction?

- All intoxicating substances are made of molecules that are shaped much like the brain's natural neurotransmitter molecules.
- A neurotransmitter is simply a messenger molecule that activates a pathway or network of neurons in the brain.
- Several neurotransmitters are affected by addictive substances, but at the most basic level, most end up activating the ventral tegmental area (VTA) and the nucleus accumbens (NAc) – the pleasure centers of the brain.

Brain structures and addiction

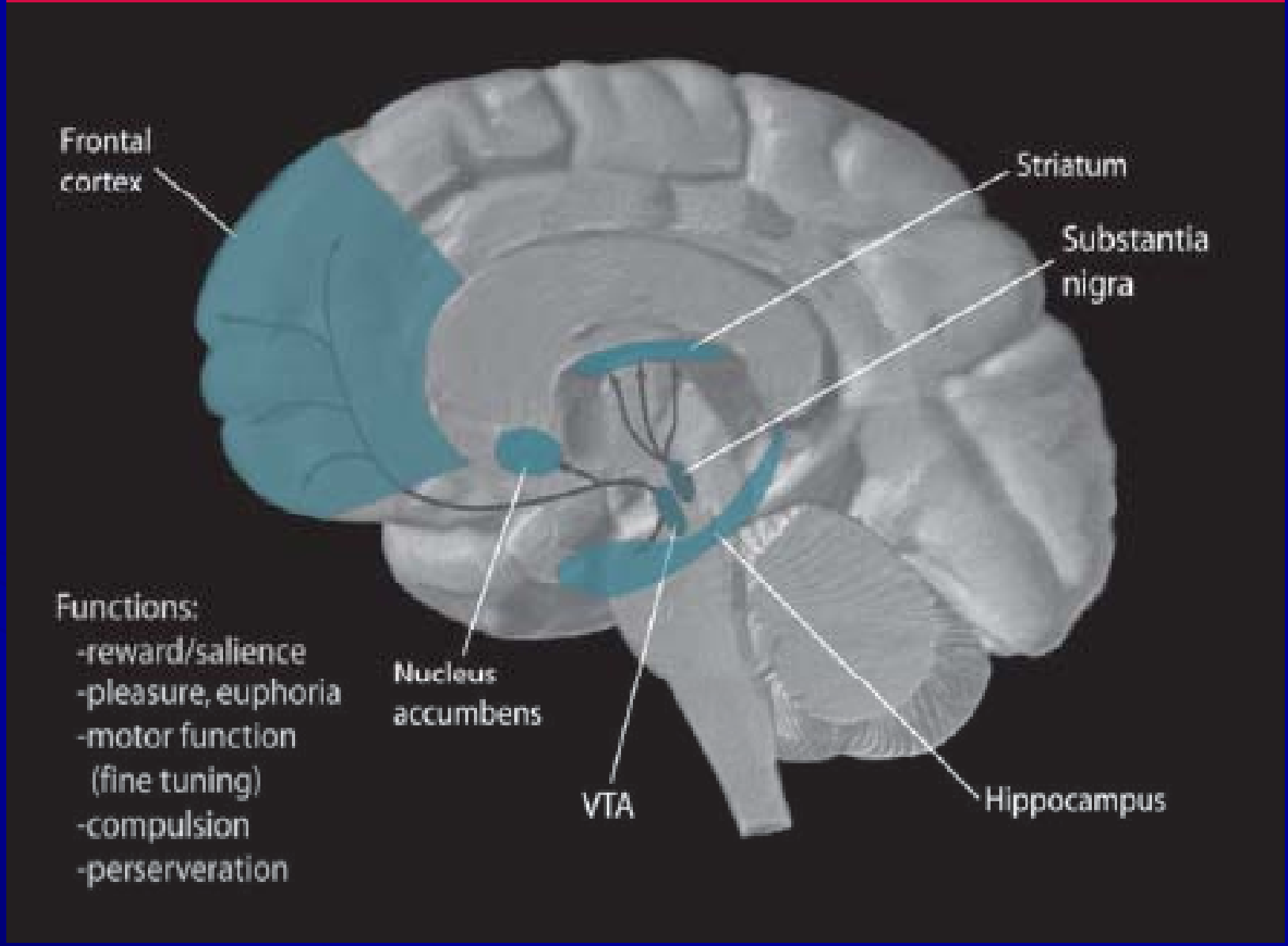
- The human brain has reward centers that mediate the experience of pleasure.
- The ventral tegmental area and the nucleus accumbens are the primary locations for core pleasure experiences.
- When a person experiences pleasure from chocolate, a ride in a fast car, a buzz off a drug, the nucleus accumbens has been activated.

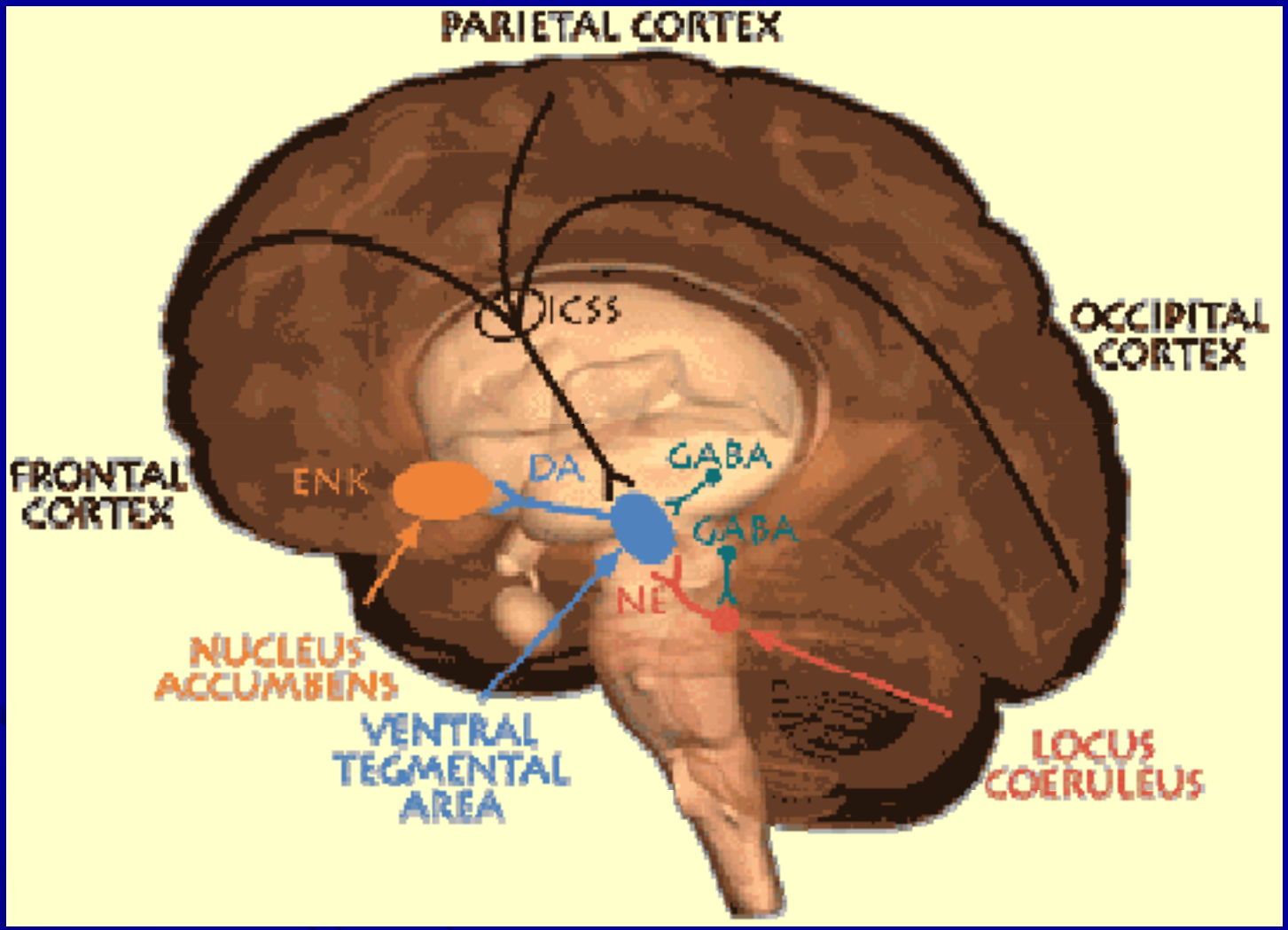
VTA and NAc

- Reward-seeking is facilitated by the release of the neurotransmitter dopamine in the nucleus accumbens (NAc),

- Subpopulations of NAc neurons even respond to predictive cues to promote reward-seeking behavior. Even cues about a drug can mobilize brain centers to begin pleasure expectations.

Dopamine Pathways





ICSS= Intracranial self stimulation

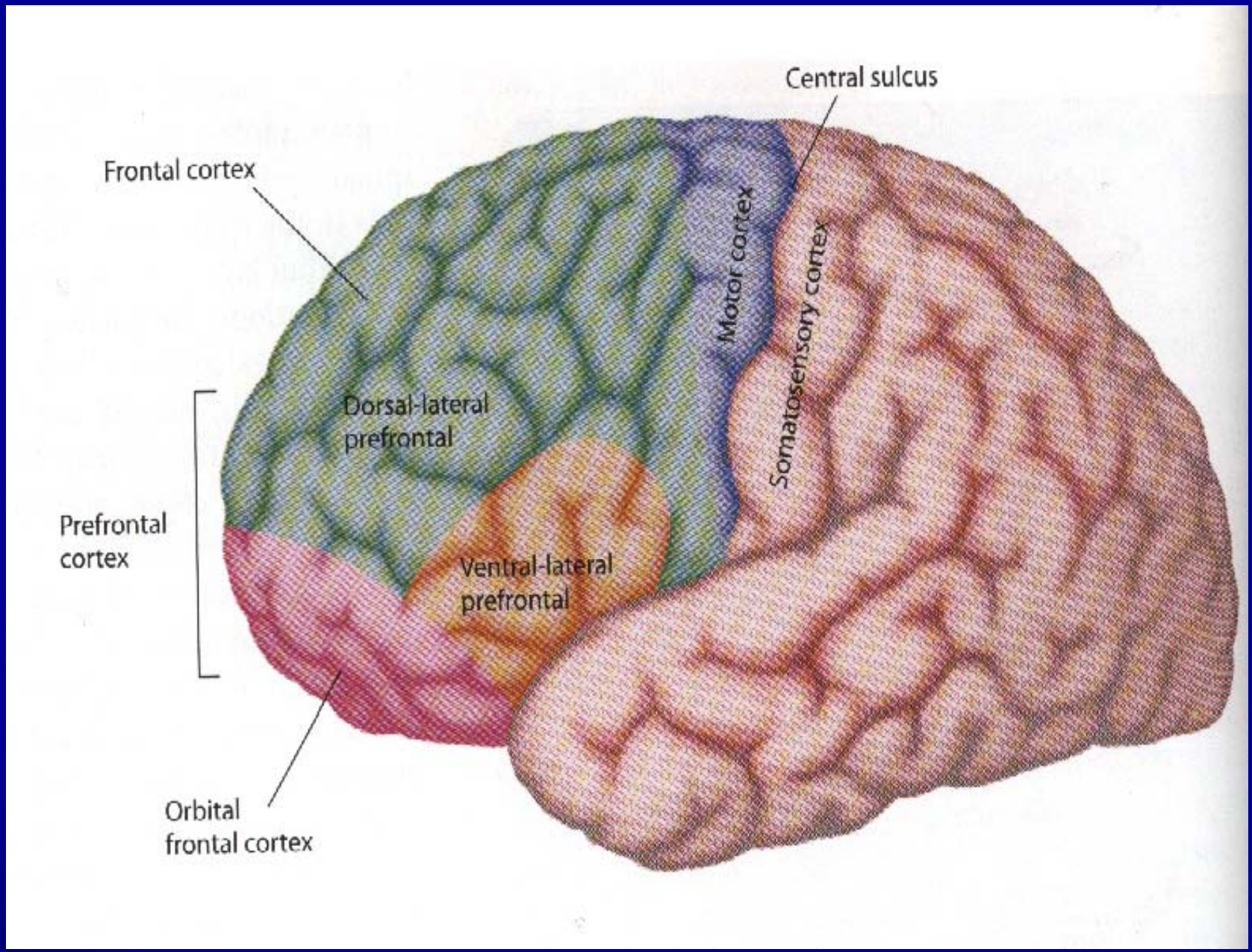
ENK = encephalin

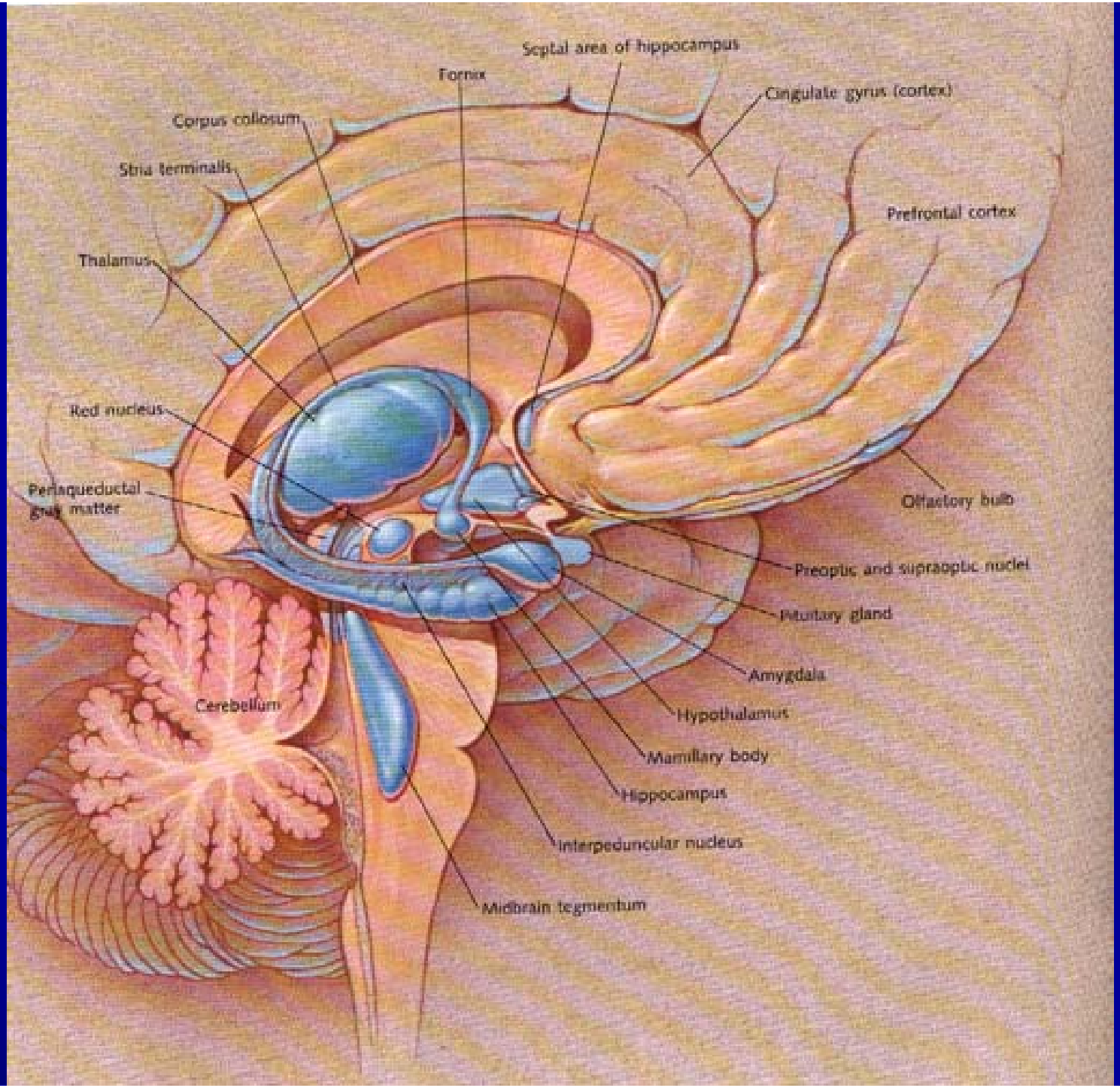
DA= Dopamine

GABA= γ-aminobutyric acid

NE= Norepinephrine

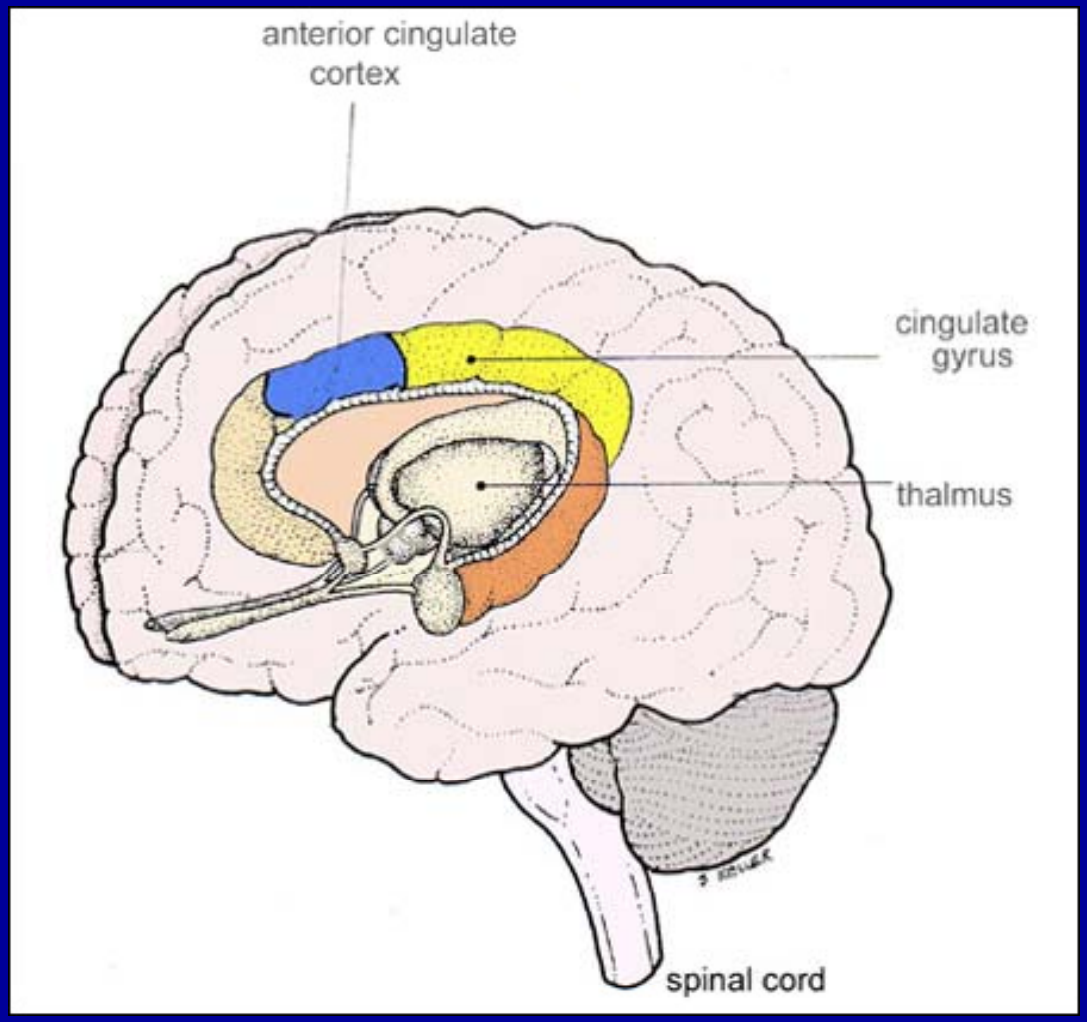
Bowles Center for Alcohol Studies at UNC
http://www.med.unc.edu/alcohol/research/Crews/brain.gif


Central sulcus
Frontal cortex
Motor cortex
Somatosensory cortex
Dorsal-lateral prefrontal
Prefrontal cortex
Ventral-lateral prefrontal
Orbital frontal cortex


Septal area of hippocampus
Fornix
Cingulate gyrus (cortex)
Corpus callosum
Stria terminalis
Prefrontal cortex
Thalamus
Red nucleus
Periaqueductal gray matter
Olfactory bulb
Preoptic and supraoptic nuclei
Pituitary gland
Amygdala
Cerebellum
Hypothalamus
Mamillary body
Hippocampus
Interpeduncular nucleus
Midbrain tegmentum

In addition to the internal structures that mediate reward experiences, the anterior cingulate cortex (ACC) along with the orbito-frontal cortex **basically navigates among reward and consequences expectations**.

Among individuals with addictions, the ACC is hypoactive, suggesting diminished capacity to do the kind of sorting out among rewards and punishments that could be expected from using drugs.

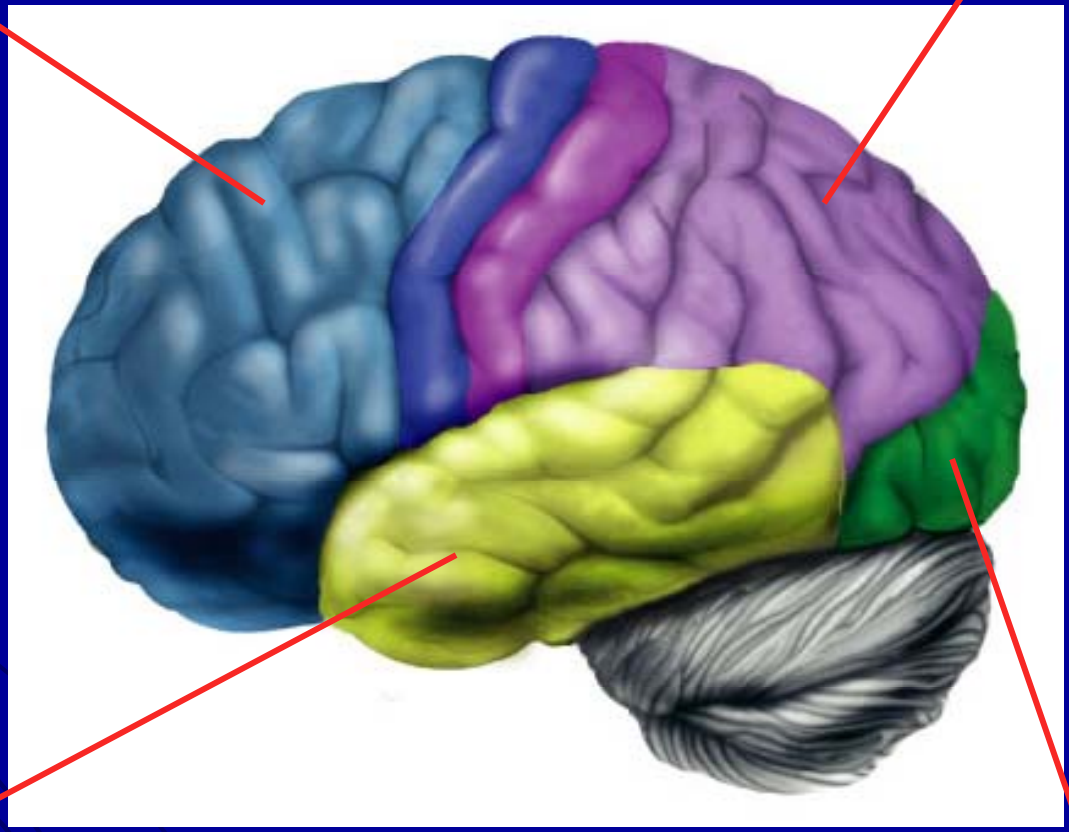


Frontal lobe

-voluntary control of skeletal muscle
-personality
-higher intellectual processes
(concentration, planning, and decision making)

Parietal lobe

cutaneous and muscular sensations
understanding speech
formulating words to express yourself



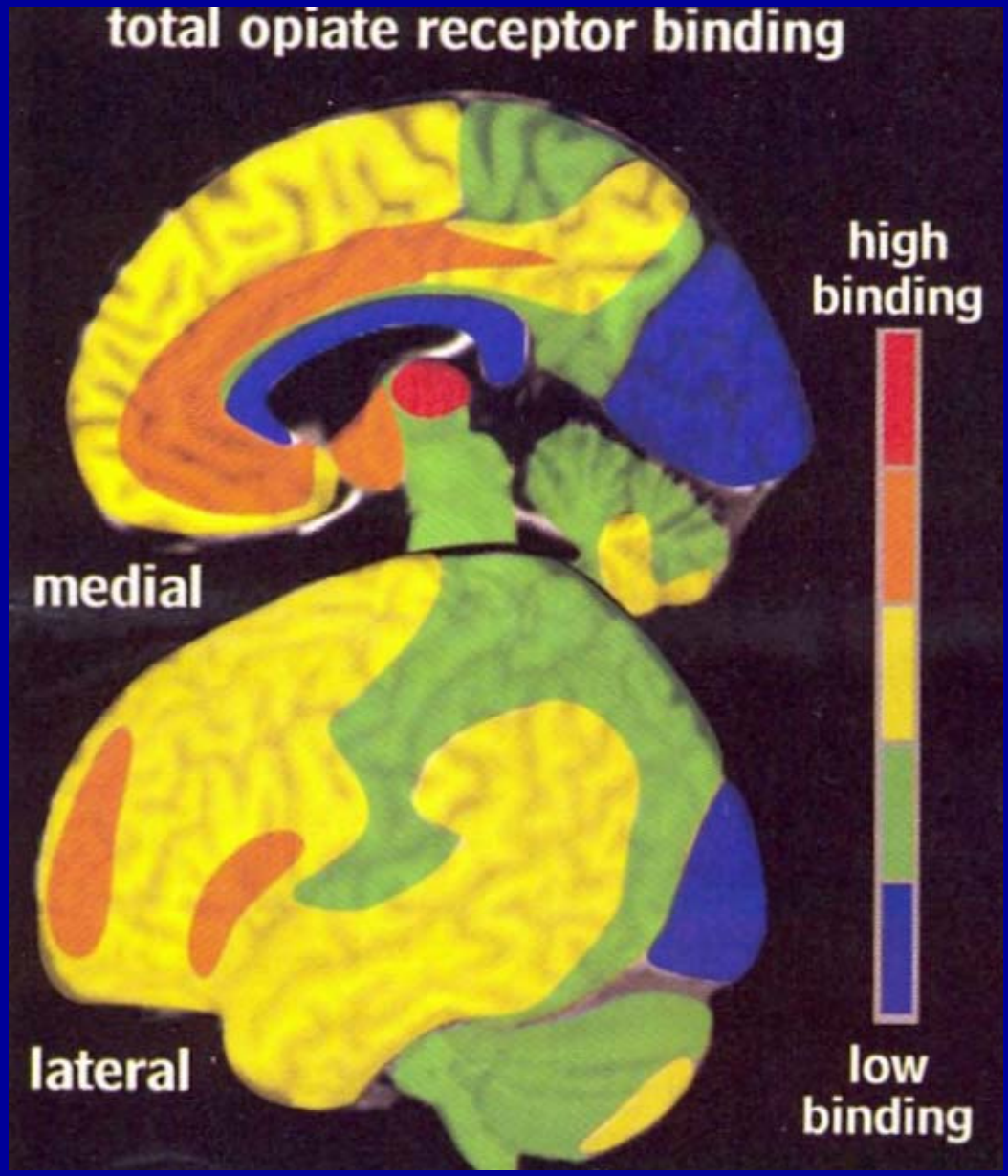
Temporal lobe

interpretation of auditory sensations
storing (memory) auditory and visual experiences

Occipital lobe

integrates movement in focusing eye
conscious perception of vision

This slide shows the specific regions in the brain where opiate receptors are particularly prevalent.



Brain and habituation

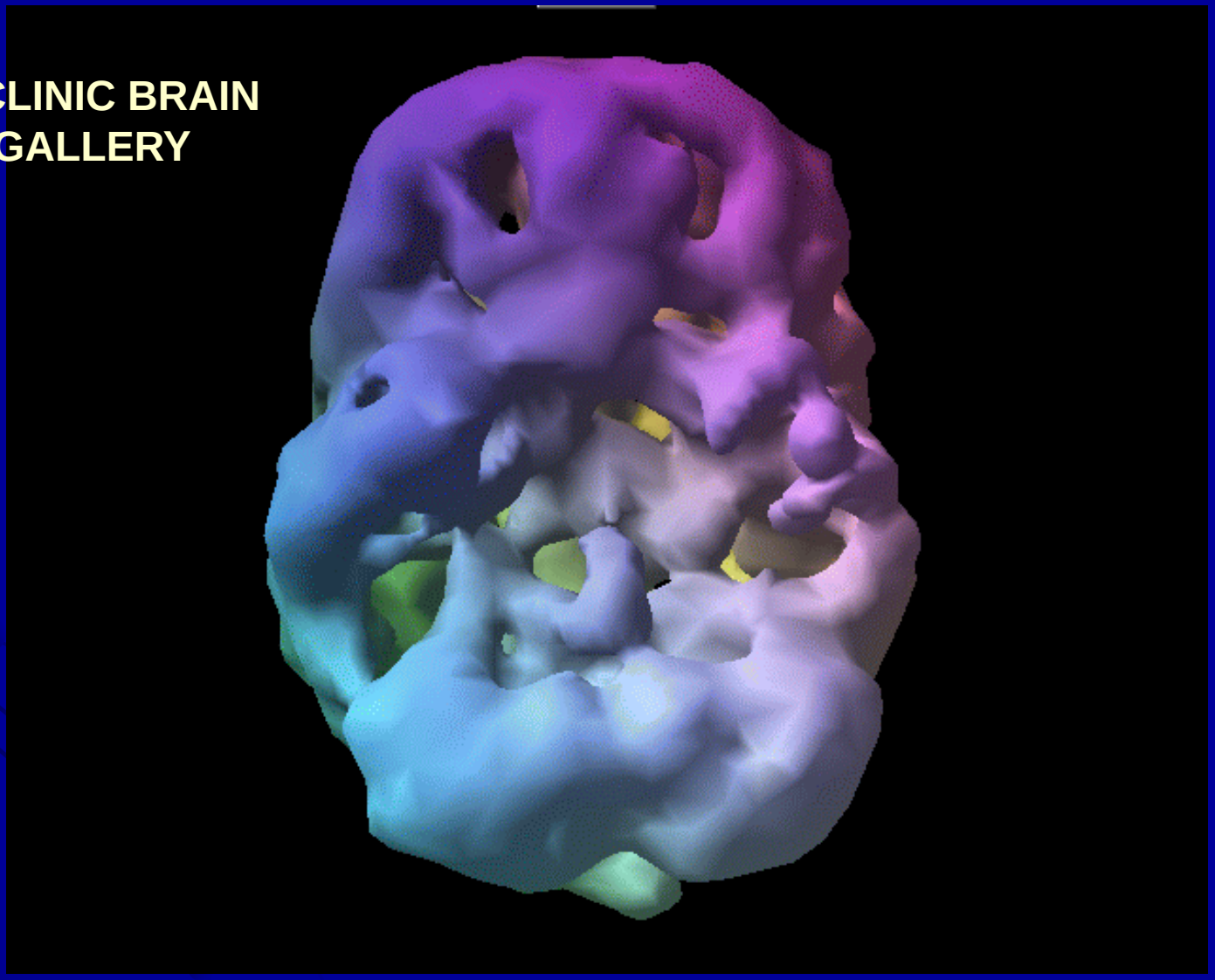
- The brain consists of millions of “circuits” and pathways.
- The more a particular pathway is “exercised”, the greater the “strength” of that pathway and the more it begins to dominate mental space.
- However, with neurotransmitters, when an excess is added to the brain system, the brain tries to compensate by getting rid of the excess. So, the more you import, the harder the brain works to get rid of the excess.
- Over time, the whole distribution of neurotransmitters gets out of kilter and the person can only function when importing the desired neurotransmitters to activate the pleasure parts of the brain.

Effects on Brain Activity

- Various approaches to functional brain imaging have been used to study specific areas of the brain in relation to the whole.
- Brain activity can be measured by examining how glucose is being metabolized by regions of the brain.
- It can also be studied by FMRI for functional anatomy and by SPECT to assess regional brain metabolism.
- These approaches allow one to examine specific areas affected by substance use.

Drug user’s brain from the under side

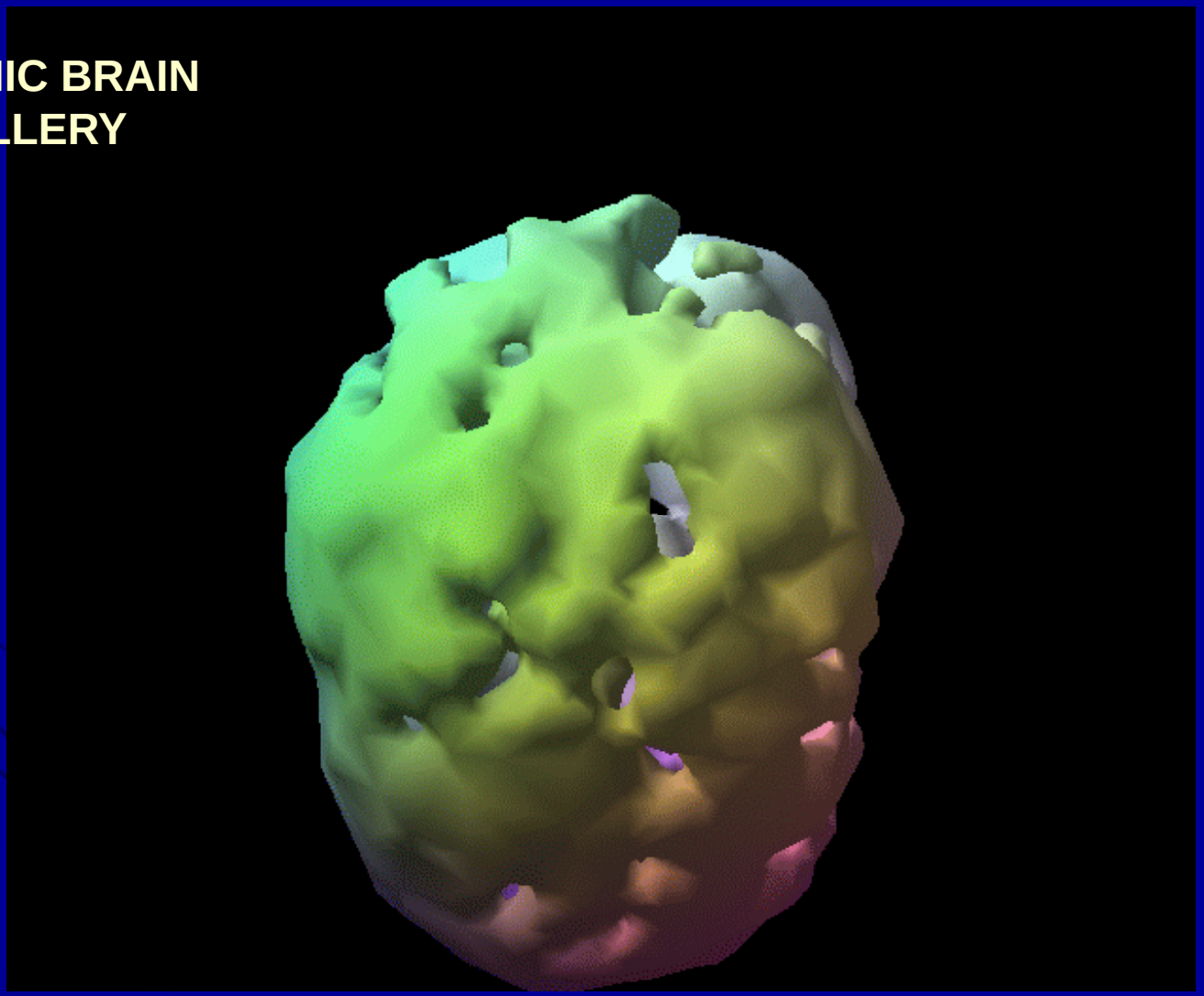
AMEN CLINIC BRAIN SPECT GALLERY



http://www.amenclinic.com/bp/spect_rotations/viewimage.php?img=da_CS.gif

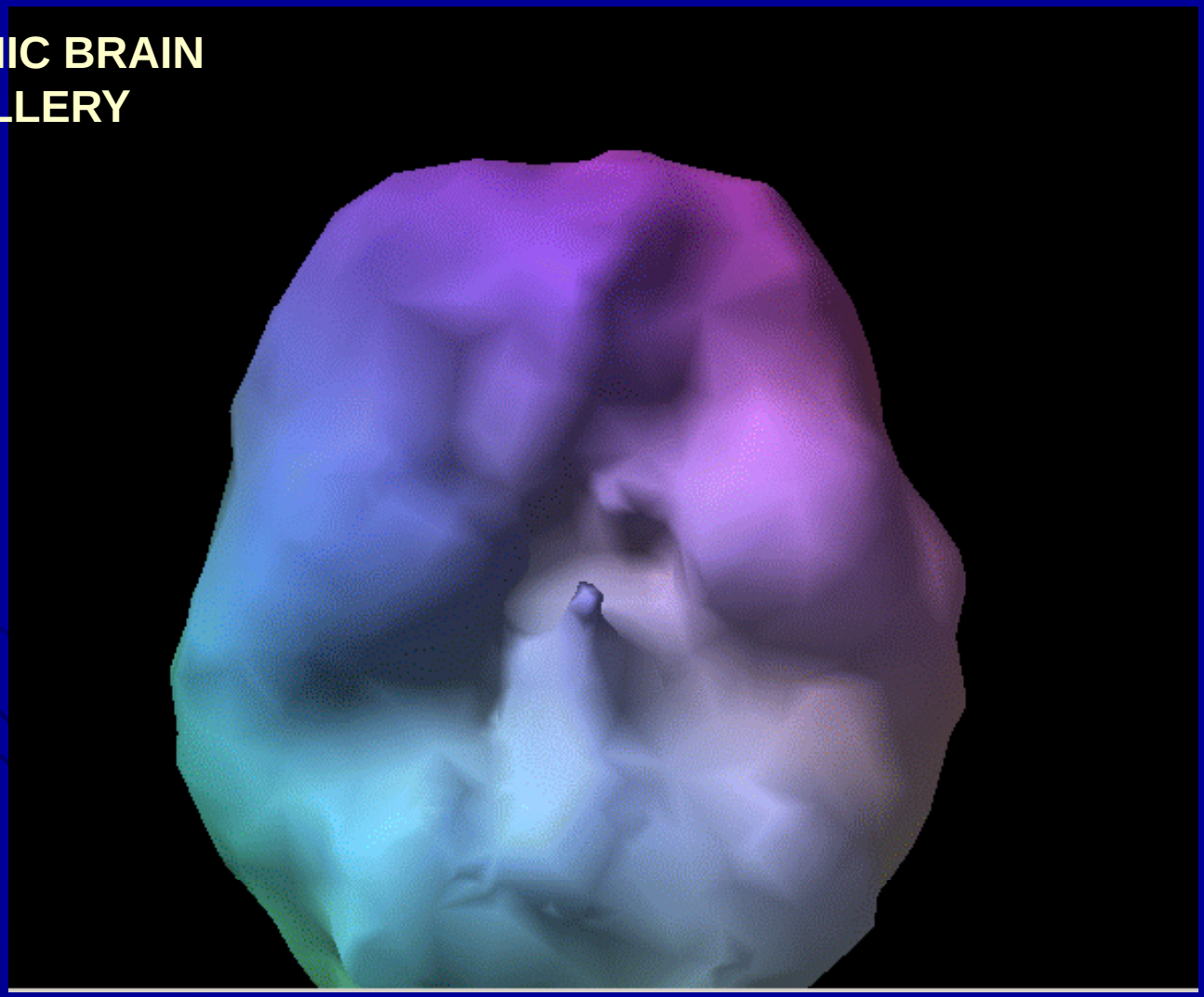
Drug user’s brain from the top

AMEN CLINIC BRAIN SPECT GALLERY



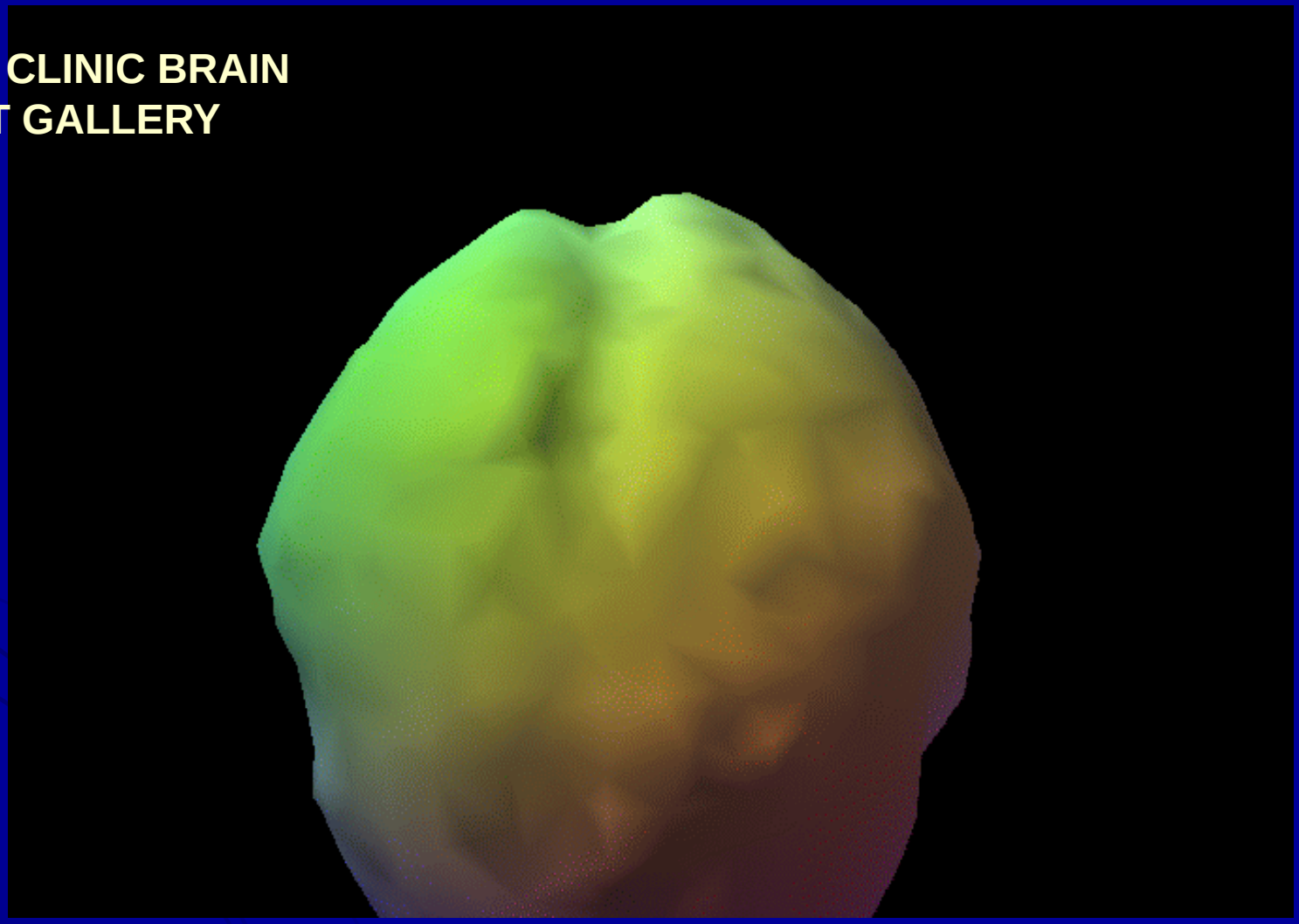
Healthy brain from the underside

AMEN CLINIC BRAIN SPECT GALLERY



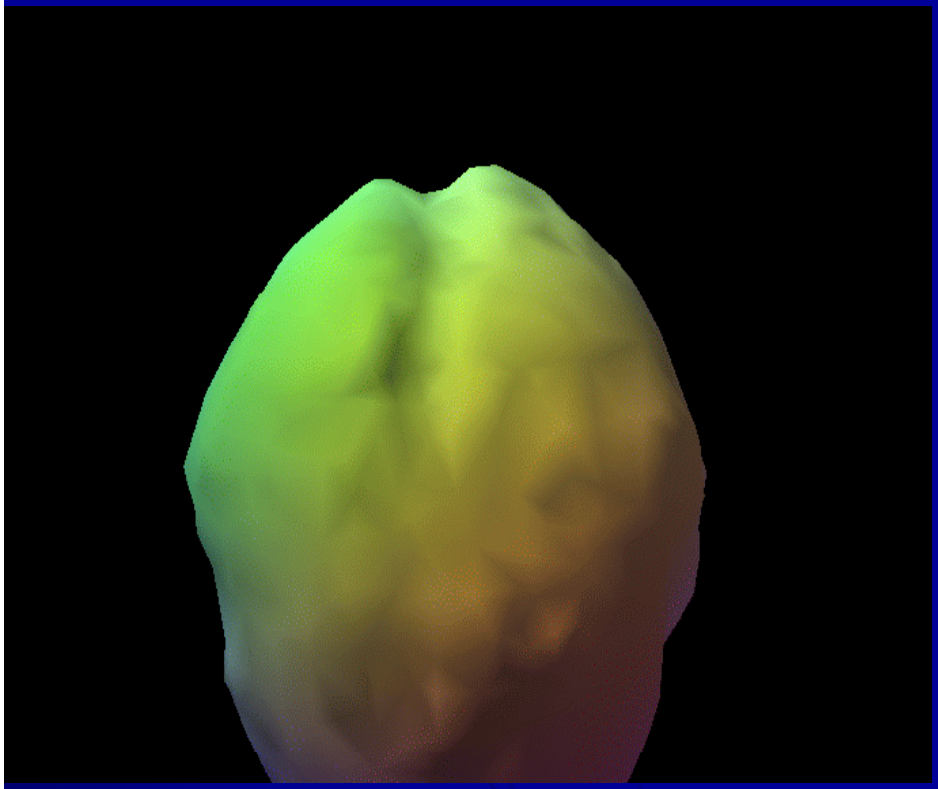
Healthy brain from the top

AMEN CLINIC BRAIN
SPECT GALLERY

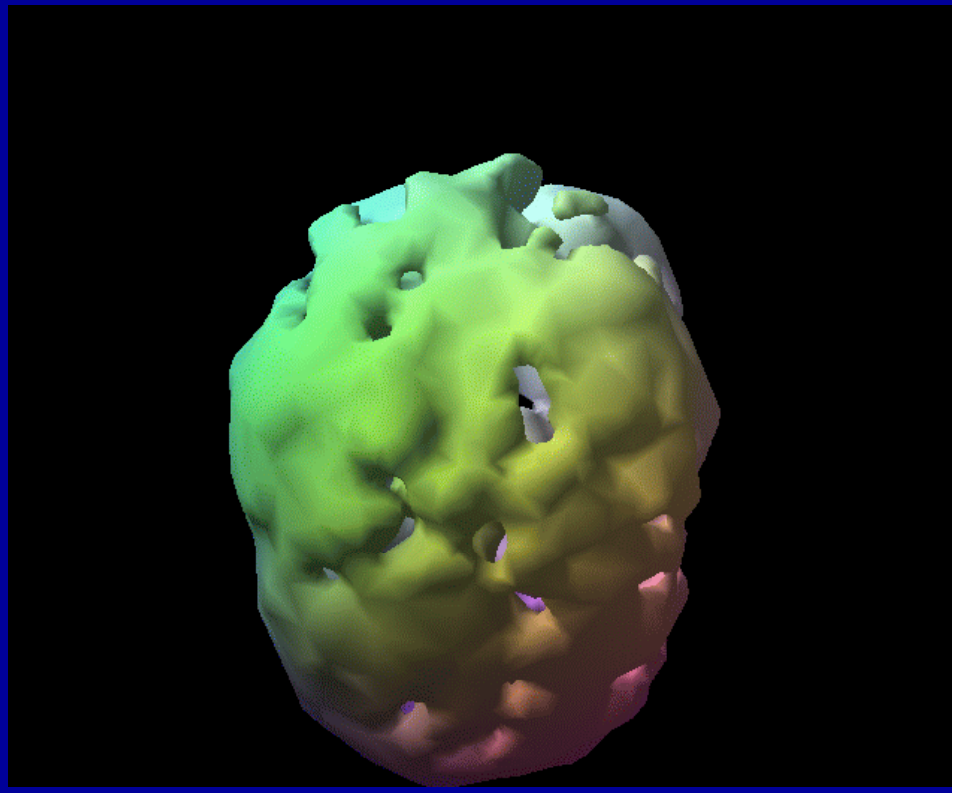


Side by Side

Healthy



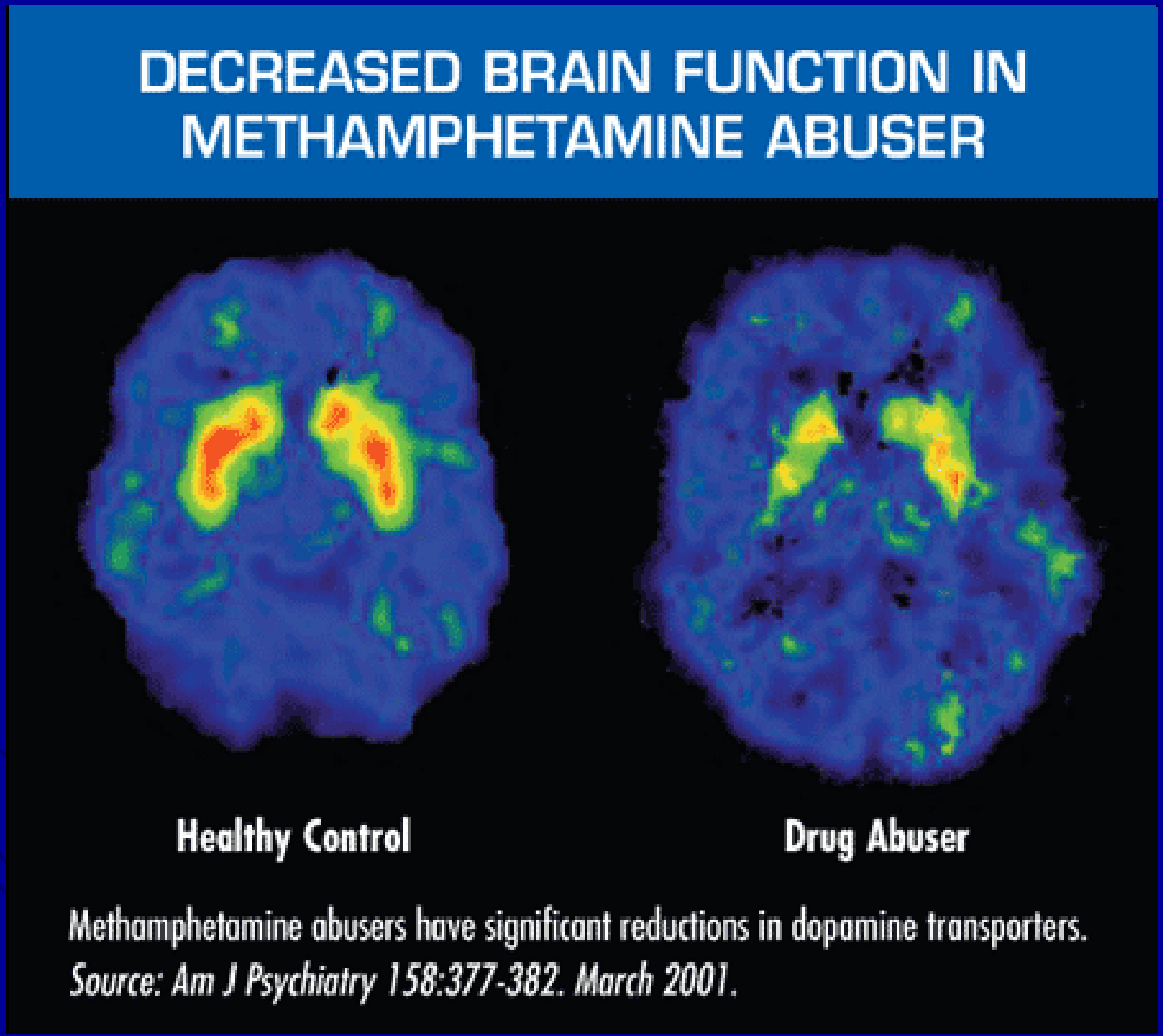
Drug User

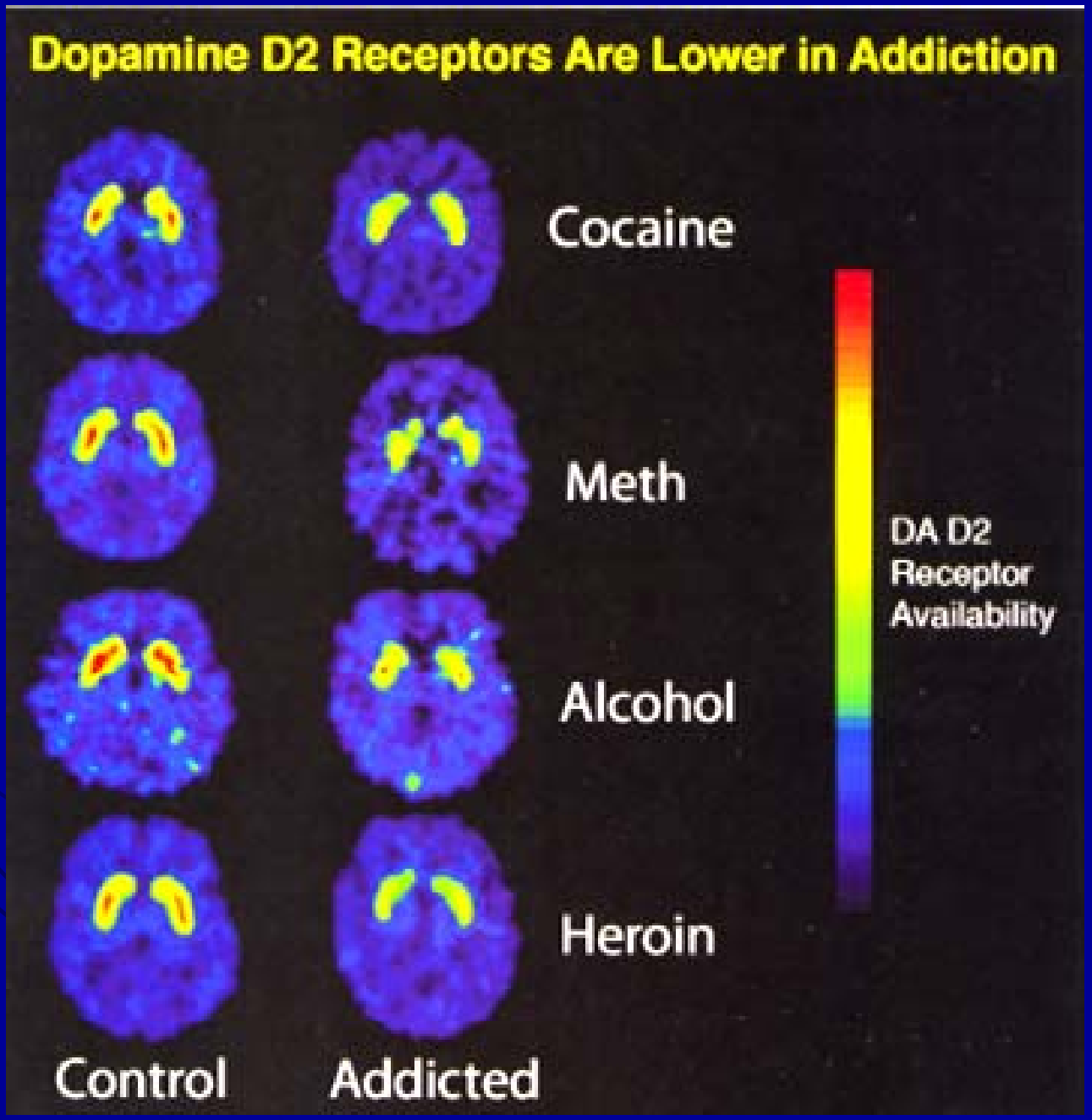


Genetics

- Evidence has been found for a genetic influence on alcoholism, opiate dependence and, less robustly, other CNS depressants such as tranquilizers.
- Genes do not make the disorder; they merely present an increased vulnerability to having the disorder.
- Genetic vulnerability to depression and anxiety can also contribute to a vulnerability to drug dependence.
- Gene expression can also be altered by life experiences as with chronic severe depression.

The meth user's brain (drug free) shows lower levels of dopamine because the brain has learned how to accommodate the high levels of artificially induced dopamine.



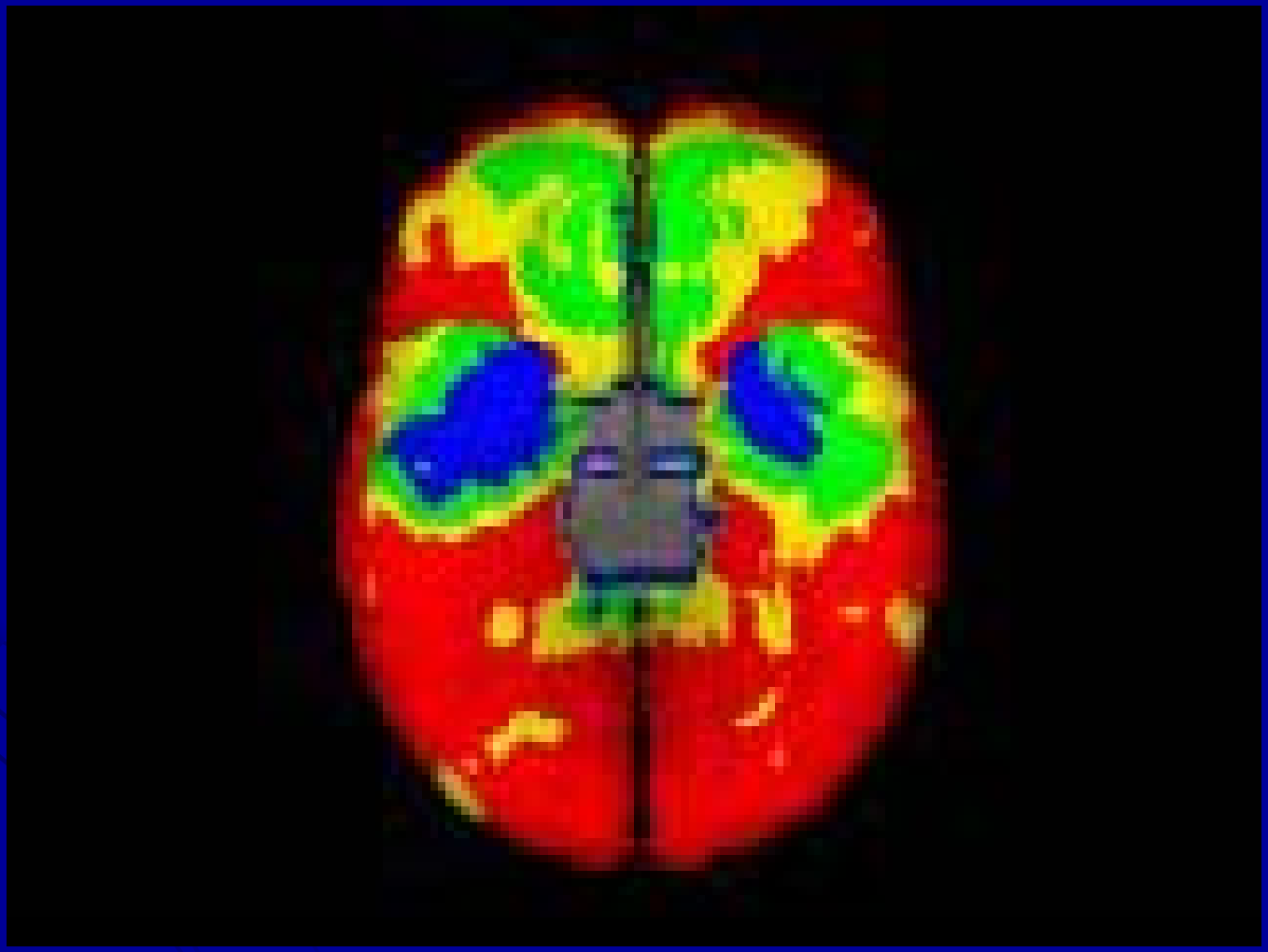


NIDA – Division of Clinical Neuroscience and Behavioral Research, NIDA NOTES, 21,(4), October, 2007

Brain functioning under other insults- similarity to addiction

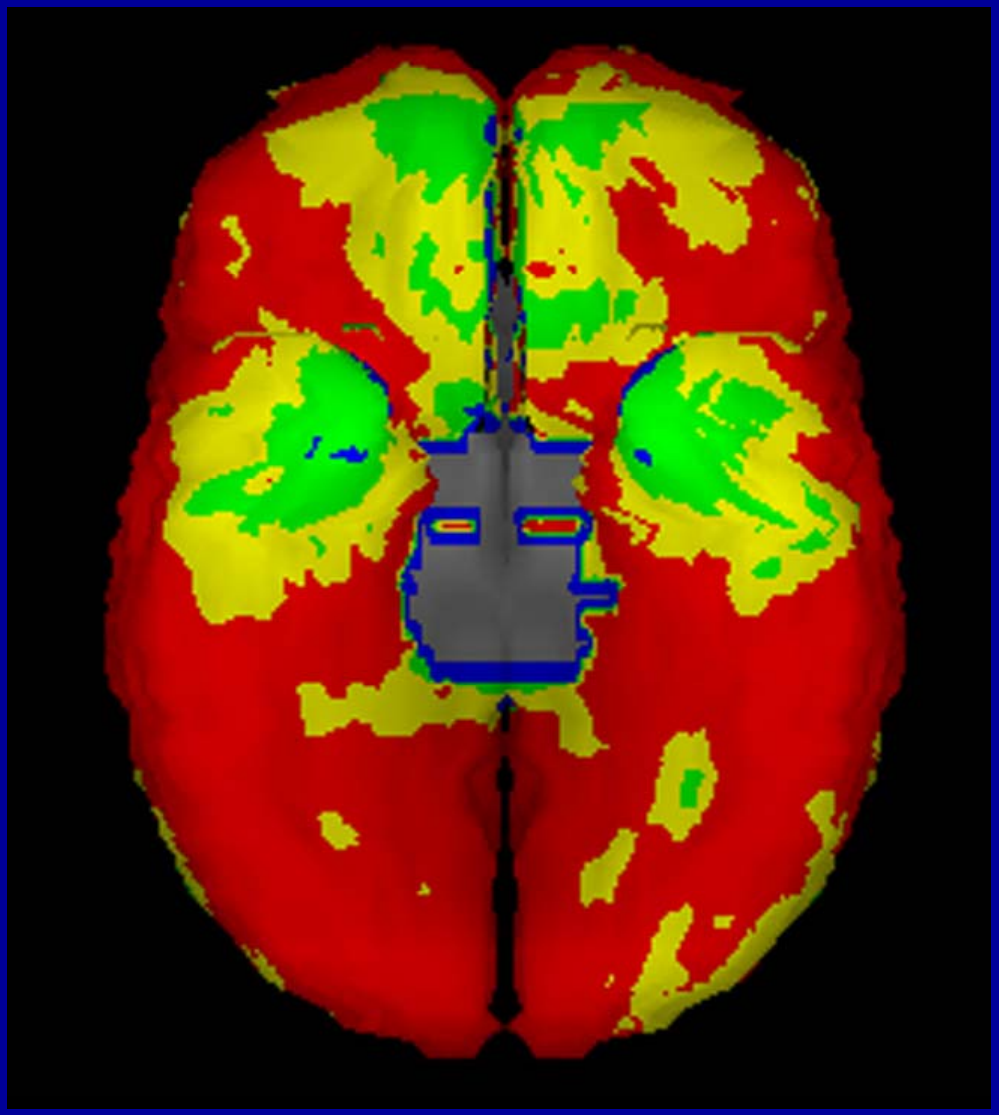
- The long term effects of substance use and even long term untreated depression can reduce frontal lobe functioning in the human brain.
- The frontal lobes are where planning, executive functions, emotion management, and reasoning occurs – AND this is the area of the brain that *most needed for recovery activities*.
- In addition, head injuries can produce similar effects on the frontal lobes.

Underside view of a depressed brain – see the yellow and green areas at the frontal lobe area showing decreased activity there.



Picture courtesy of Dr. William Klindt of Silicon Valley Brain SPECT Imaging, San Jose, California www.braininspect.com

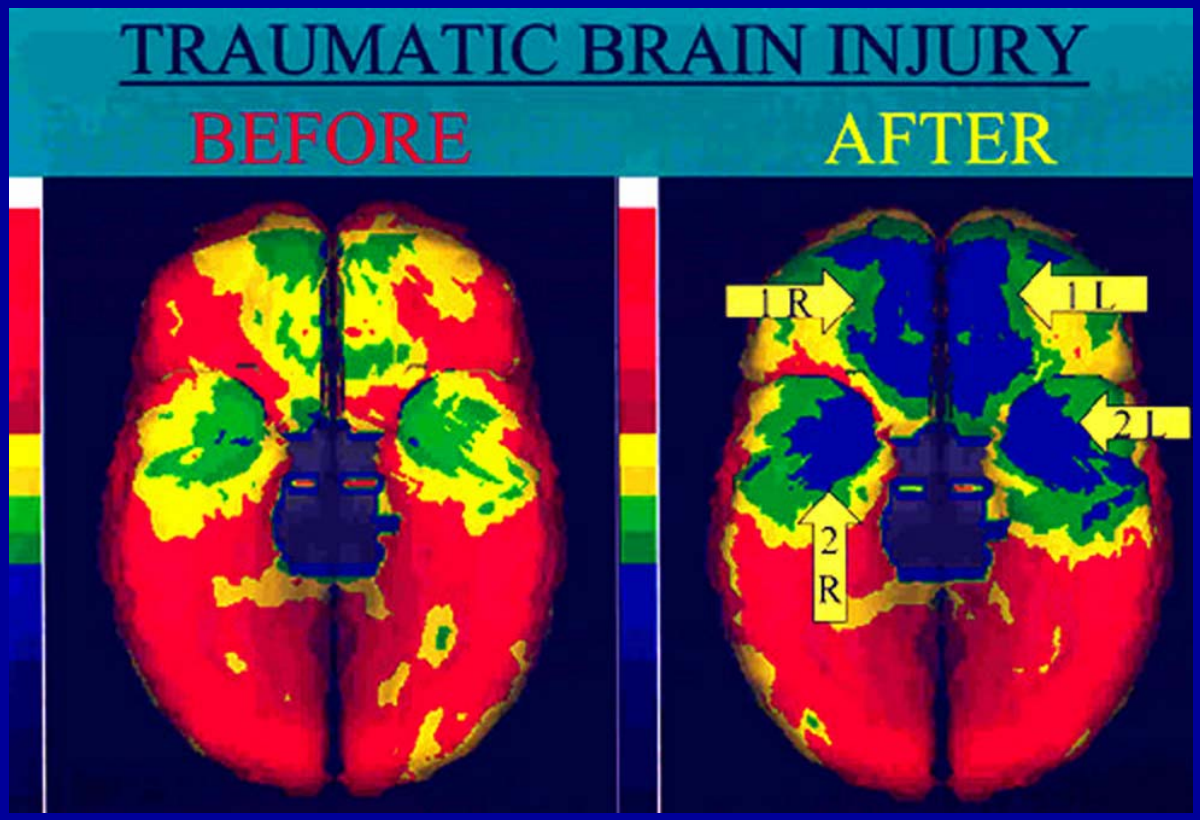
Now, for comparison, look at this same view from the underside of a brain that has had frontal lobe injury in an auto accident. The yellow and green colored areas are where there is less brain activity.



Picture courtesy of Dr. William Klindt of Silicon Valley Brain SPECT Imaging, San Jose, California www.braininspect.com

Brain injury and addiction can actually result in similar effects on brain activity – particularly in the frontal lobes where decisional thinking occurs

Here in this set of images, you can see a pre-injury and post injury difference in blood flow. The blue, yellow and green areas are where there is less brain activity – that is where the injury was.



Picture courtesy of Dr. William Klindt of Silicon Valley Brain SPECT Imaging, San Jose, California
www.braininspect.com

More on Genetics

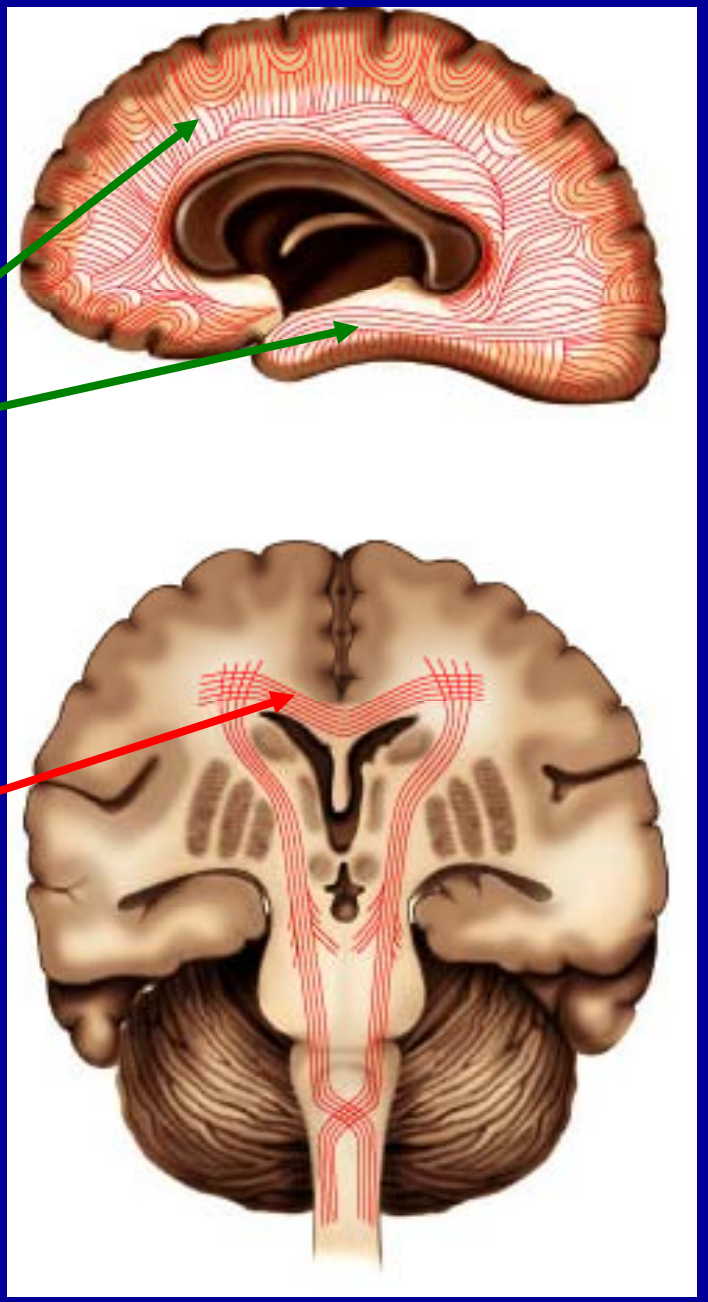
- Basic neurochemical functions in the human brain may be “set” by genes.
- Some people are born with “imbalances” of certain neurotransmitters such as serotonin.
- Chronic lower levels of serotonin may result in vulnerability to substance abuse – hence the concern about depression and substance abuse or dependence.

Drug use and neuro-vulnerabilities

- Much of the thinking is that brains that lack sufficient neurotransmitter availability may be vulnerable to drugs that help compensate for vulnerability.
- Likewise, some brains may simply be more sensitive to the euphoriant effects of certain drugs.
- For example, opiates for most people are distasteful, causing vomiting and a foggy feeling. For those who have a particular mu-opioid receptor site gene (A118G), the opiate produces a feeling of wholeness and peace in the world.

Association tracts: connect neurons in same area – these pathways can be affected during fetal development when the mother uses alcohol. In addition, alcohol use during fetal development can affect how well neurons migrate to their propose place in the brain.

2. Commissural tracts: that connect neurons in one cerebral hemisphere with neurons in the contra-lateral (opposite) hemi-sphere, ie. the **corpus callosum**



Are the changes from drug use permanent?

- Nope. Yep.
- There is increasing evidence of brain recovery from certain kinds of addiction.
- Long term heavy alcohol use results in some permanent damage and alcohol is perhaps the most harmful drug to the CNS.
- However, much of the damage done by alcohol use can be either restored or the brain can develop compensations for damaged areas.
- Even with methamphetamine, there is evidence of correcting earlier CNS damage.
- However, fundamental neurochemical “imbalances” that were there before the addiction, may still need attention.

Recovery of Brain Dopamine Transporters in Chronic Methamphetamine (METH) Abusers

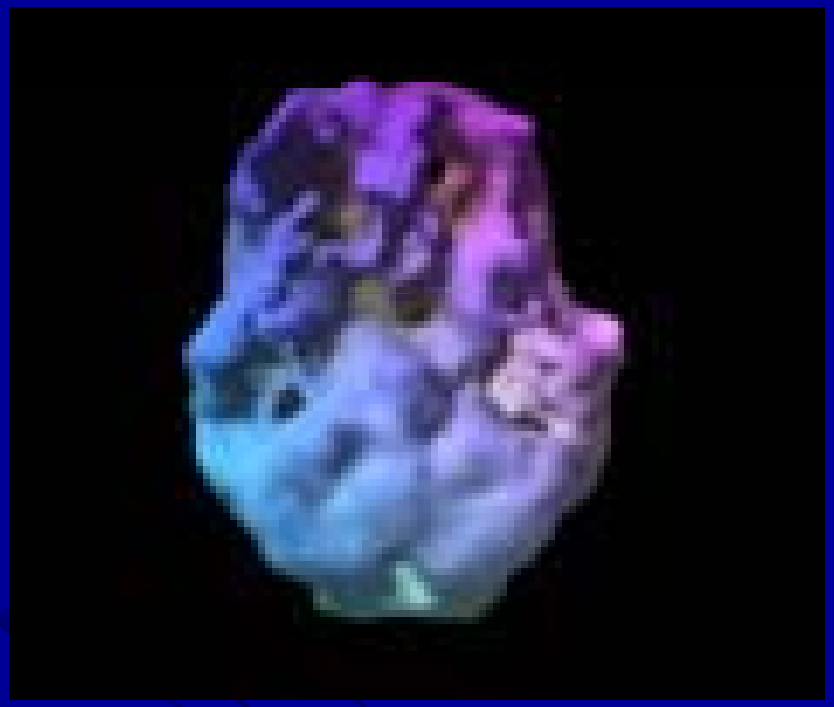
Normal Control

METH Abuser
(1 month abstinence)

METH Abuser
(24 month abstinence)

Source: Volkow ND et al., *Journal of Neuroscience* 21:9414–9418, 2001.

Imaging the underside: Extensive HX Alcohol and Cocaine – Before and After TX



Before

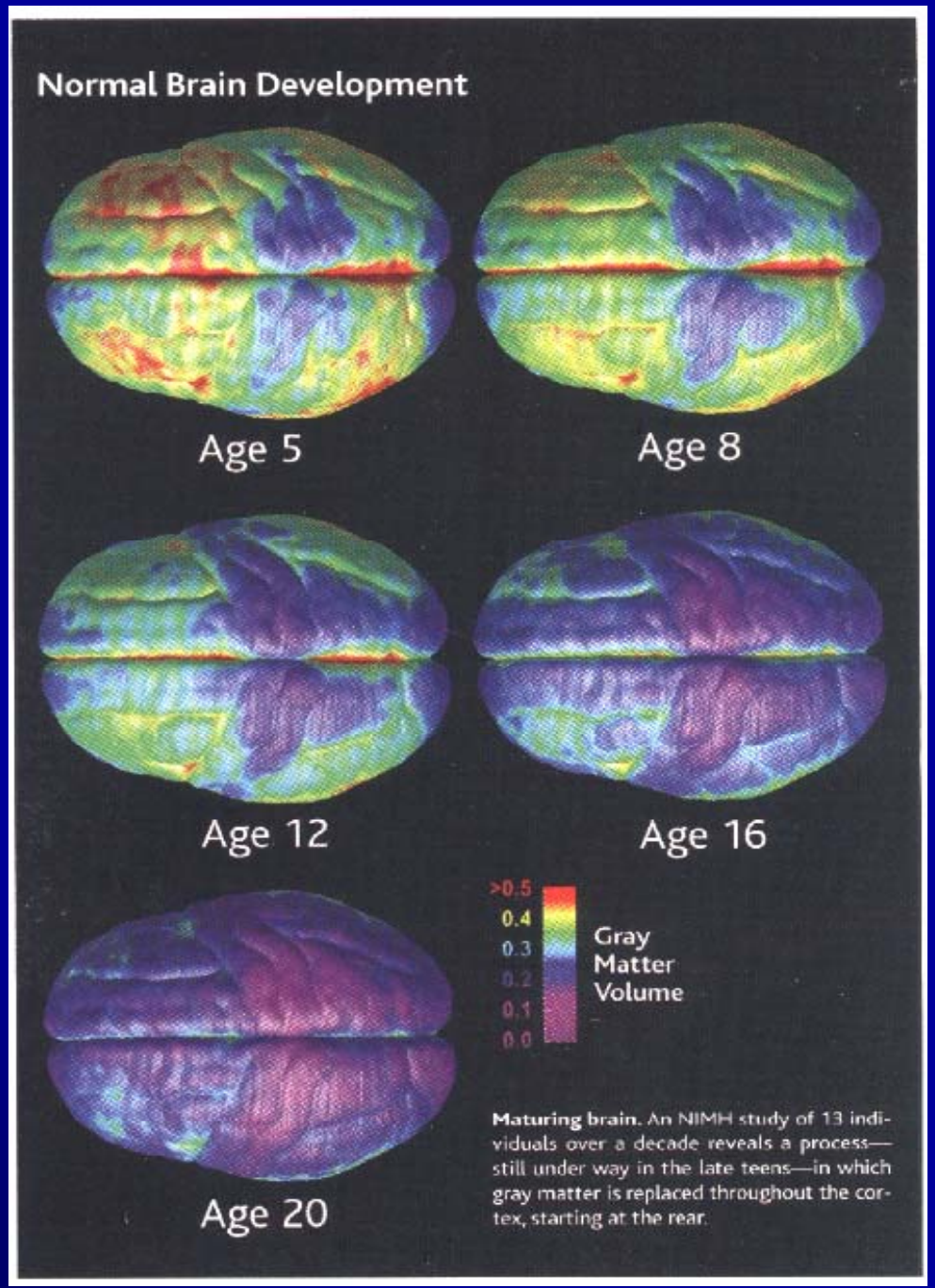
After

Do all drugs work the same?

- Nope. Yep.
- Each substance mimics a particular neurotransmitter, but in the end, each of these trigger a cascade of chemical events that results in activation of the VTA and NAc.
- If the event did not end up in the VTA/NAc, the substance would not be addicting.

The brain, drugs, and developmental stages

- The brain's capacity to adapt to substance use is also very different depending on the individual's age in the developmental cycle.
- The brain is constantly changing and even more so from birth to about age 20 or 21.
- There are major advances in development of the higher cortical areas during adolescence and substance use prior to this last stage of major brain development has serious consequences for continued development.



This set of images, a composite of 33 brains during development, shows how the cortex goes through changes during adolescence. The purple color shows the replacement of gray matter in the cortex throughout development. By age 20, the brain is essentially complete in cortical development.
(Science, 2002).

So, what about the behavioral effects?

- Since drug abusers and addicts do not overtly seem "crazy" it seems natural to expect them to wake up and quit using – particularly when they have experienced major problems due to drugs.
- But, the areas of the brain that do self-reflection, assessment, planning, and careful listening to feedback are all damaged by substance use.
- Furthermore, the addict loses the ability to invent solutions to problems.
- The frontal lobes are greatly affected by almost all substances – both short term and longer term.
- Thus, the very thing we are asking them to do is the one thing they will have the greatest difficulty doing.
- It's like asking someone with sprained ankles to run.

What is affected?

- Everything.
- The emotional systems of the brain are ungoverned and run rampant.
- The physical sensation part of the brain gets badly distorted – differently for different substances.
- Thinking gets completely re-wired as the “normal” thinking areas get shut down.
- Everything gets oriented around feeling okay – feeding the craving and getting high to feel “normal” again.

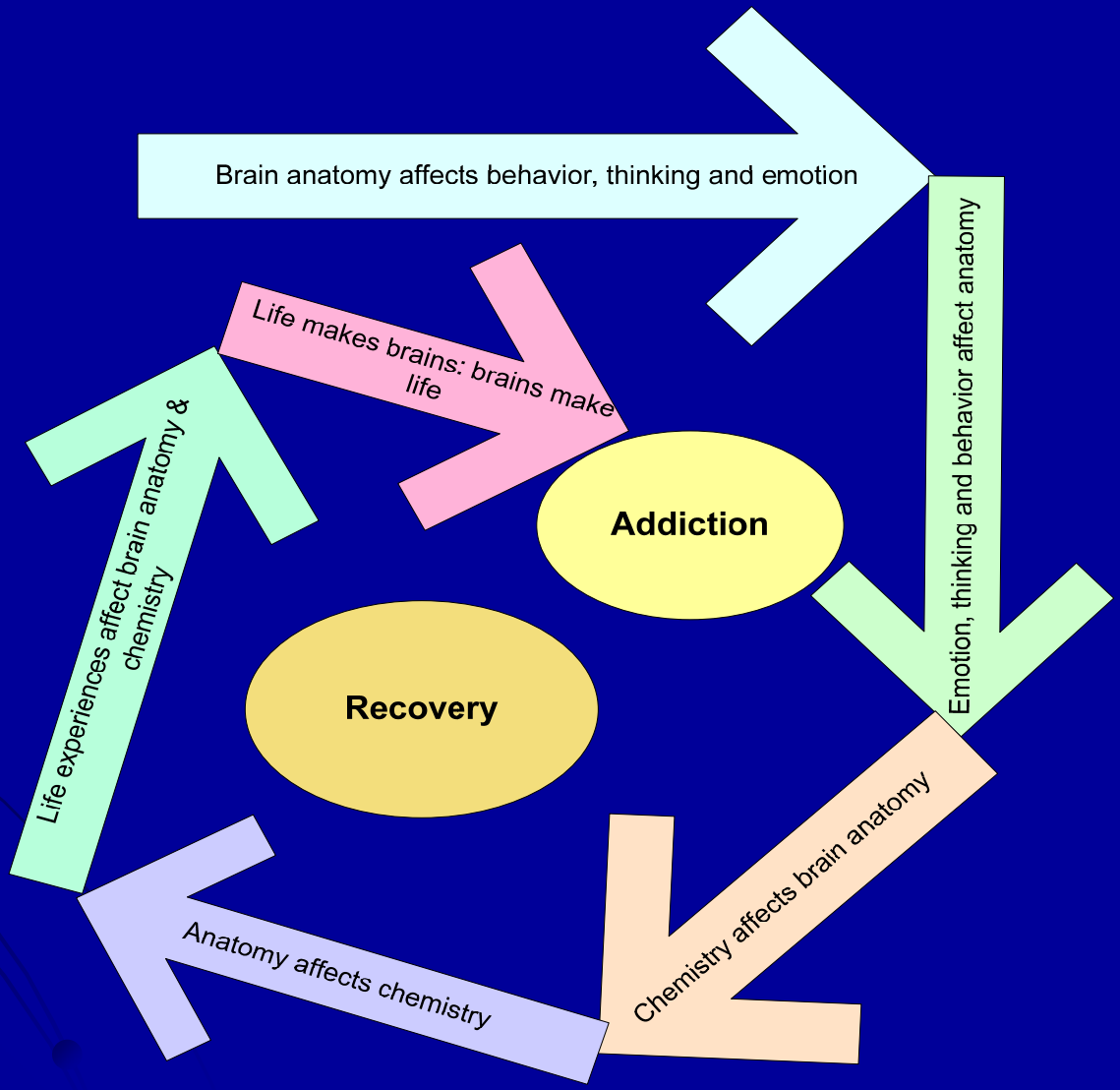
Why can’t they just stop?

- Remember, each intoxicating substance mimics a natural chemical. The more you introduce into a brain, the more the brain tries to compensate.
- So, for example, when using methamphetamine, the brain in deluged with dopamine and norepinephrine. The brain tries to clear these chemicals out using enzymes that break them down and the brain develops ways to increase production of these enzymes. Also, the nerve cells develop more receptor sits to handle the increases number of NE molecules.
- Thus, when the user goes “cold turkey” the mass of enzymes and the greatly increased number of receptor sites cause massive depletion of dopamine and norepinephrine – so much so that even basic capacity is seriously affected.
- This is what fuels craving in the brain.

So, what about the implications of all this science?

- The neurobiology of addiction suggests a complex, genetically vulnerable condition.
- Brain habituation means that core vulnerabilities have also been increased due to the brain's compensatory processes.
- Therefore, to go cold turkey means the brain becomes like a fish on the beach.
- Science largely agrees with many counselors in the field in seeing *substance dependence* as a *disease process*. *Substance abuse* is less clearly identifiable as a disease because it is less severe, has less clear effects on overall functioning, and can have much more diverse treatment outcomes.
- Clearly recovery means a long time for re-training the brain, reconditioning it to function in the absence of the imported substance.

The role of brain in addiction: The role of self in addiction



Terms

- The popular term “addiction”, captures the clinical term “dependence” and has been used in this presentation for that reason.
- Recovery is used here to mean managing substance dependence or addiction.
- Recovery is something a person does, it is not what someone does for the person.
- Treatment may be used by someone as part of their recovery.
- But, as we shall see, many other things may be done by the person as part of their recovery, including closer engagement with their faith practices, using the steps of AA or NA, or re-committing to the structures of daily living.

The bottom line from the scientific point of view

- Just saying “no” is unrealistic.
- It would be comparable to telling someone with diabetes, to just “get over it.”
- Treatment may be needed and may also include medications to help the brain re-establish its equilibrium.
- In fact, some people will need long term medications to offset genetic neurochemical problems or to help the brain compensate for the lost substance.
- Some will need the newer generation of anti-craving medications or replacement medications such as buprenorphine.
- Science suggests that the idea of “moral deficiency” is inappropriate and stigmatizing.

Addiction, Dependency, Disease

- By whichever label one wants to approach addiction, science has basically suggested that it is a chronic condition that requires life-long management.
- It can be compared to Type 2 Diabetes, chronic hypertensive disease, asthma, and obesity in that all of these conditions involve a complex of physiological and behavioral health components.
- The idea that one treatment episode will resolve substance abuse, let alone addiction, is unsupportable.
- The life course of addictive disease is punctuated by multiple episodes of treatment, recovery activities, and relapse periods.

Final observations on science and addictions: Treatment

- A host of evidence-based approaches has been developed.
- The hard science behind these evidence-based approaches is still rather weak and has been done under very tightly controlled situations that cannot be found in the real world.
- However, most of the evidence-based practices build from what has been learned about addiction through neuroscience.
- **All of the identified evidence-based approaches are congruent with the neurobiological understanding of addictive disease in that all "exercise" the frontal lobes and induce learning about new ways of thinking and behaving.**

What is required for recovery?

- An understanding of co-occurring conditions
  - Victimization
  - Mental health problems
  - Health problems
  - Deprivation of capability
- Accessibility of providers
- Availability of resources
- Respect for even the limited autonomy
- Wrap-around services and goods
- Patience with relapse
- Active use of recovery supports
- An understanding of a long term process
- An appreciation of how extraordinarily difficult recovery is