UW Medicine
DIVISION OF
PAIN MEDICINE

Differentiating Dependence from Opioid Use Disorder

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Take the case of:

- Francie is a 56 yr old retired police officer.
- In 1995 she was injured in a car accident resulting in a fractured pelvis and right shoulder.
- She has had bilateral shoulder and neck pain since the injury.

- She is currently treated with Oxycontin 80 mg twice daily and oxycodone 10 mg 4 times daily (MEDD 300 mg).
- Dose has been stable for 10 years, there have been no aberrancies, and she depends on the opioid to function.

In 2007, the CDC guideline comes out

- Francie's doctor told her he was obliged to taper her to a lower dose because the dose she was currently taking is no longer considered safe.

- Multiple attempts to taper resulted in the same outcome: she reported that she was not able to function at the reduced dose and that all her previous pain had returned.

Does Francie meet criteria for OUD?

DSM-5 Criteria for Diagnosis of Opioid Use Disorder

Diagnostic Criteria*

These criteria not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Check all that apply

	Opioids are often taken in larger amounts or over a longer period of time than intended.
	There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
	Craving, or a strong desire to use opioids.
	Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.
	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
	Important social, occupational or recreational activities are given up or reduced because of opioid use.
	Recurrent opioid use in situations in which it is physically hazardous
	Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
	*Tolerance, as defined by either of the following: (a)a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b)markedly diminished effect with continued use of the same amount of an opioid
	*Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b)the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

Total Number Boxes Checked: _____

Severity: **Mild**: 2-3 symptoms. **Moderate**: 4-5 symptoms. **Severe**: 6 or more symptoms

What is opioid addiction and is opioid use disorder the same as opioid addiction?

The way most people understand drug addiction

- Loss of control over drug use
- Drug use overwhelms everything else

Opioid Use Disorder

- A term chosen by APA to use in DSM V
- Chosen as less pejorative than “addiction”
- Abandons prior progression from intermittent use through abuse to eventual “dependence” which was very confusing
- Instead, describes progression from mild through moderate to severe

http://www.dsm5.org/ProposedRevision/Pages/proposedrevision.aspx?rid=431

Opioid Use Disorder

- A lot of experts do not like or agree with DSM V OUD
- Some people consider only severe OUD (ie meets 6 or more criteria) as equivalent to ”addiction”
- Some people consider that pain patients struggling to taper meet criteria for mild or moderate OUD

Criteria from American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Washington, DC. Page 541

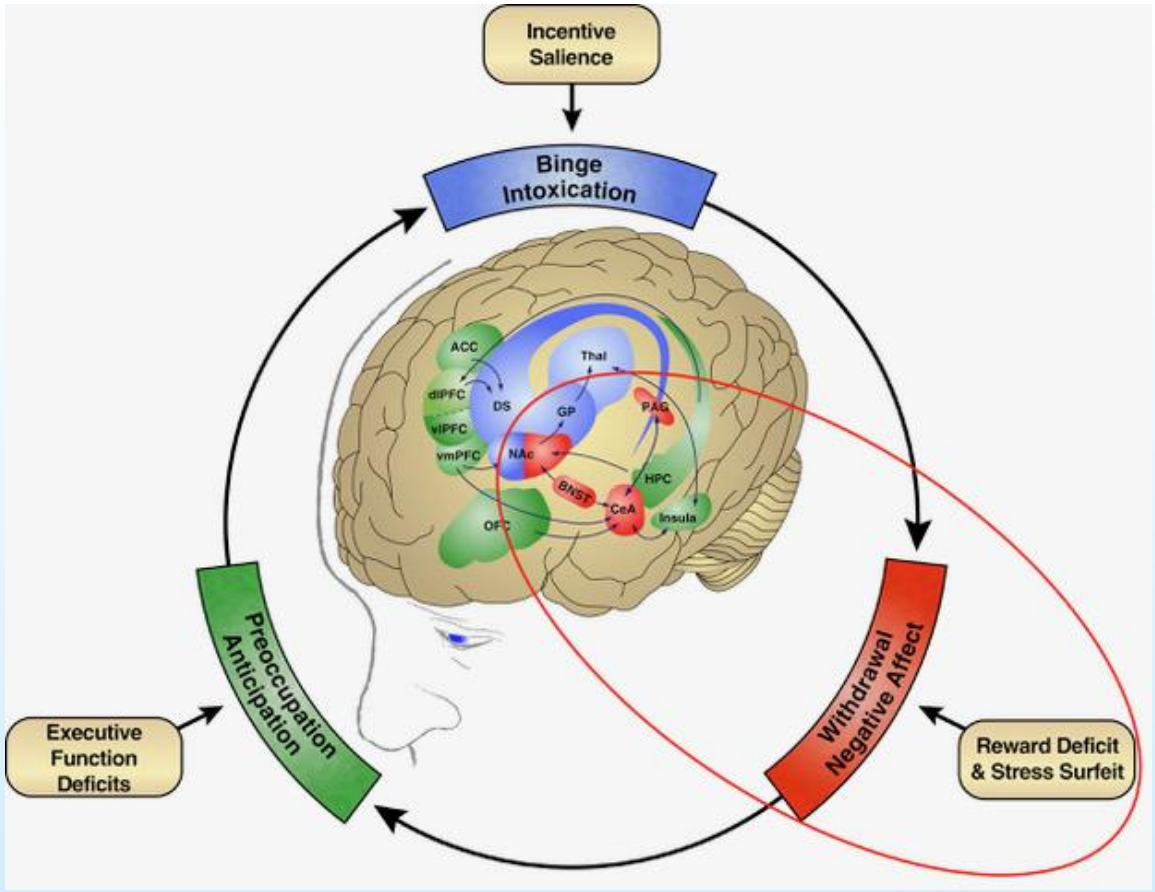
Does Francie meet criteria for OUD?

What are the reasons you may not want to apply the OUD criteria

- It doesn’t really meet any of the criteria
- The diagnosis upsets the patient
- The diagnosis carries stigma, even if less than “addiction”
- The distinctions between mild, moderate and severe are not widely understood
- There may be employment or child custody implications
- Neurobiologically, what Francie has is not addiction

Neurobiology of Dependence

- Dependence may be simple and easily reversed in some individuals, notably those taking opioid short-term or intermittently
- Prolonged, continuous opioid use produces the syndrome of Opioid Dependence



Koob & Volkow Lancet Psychiatry 2016;3:760, Ballantyne, Sullivan and Koob, 2019 (in press)

Withdrawal/negative affect stage

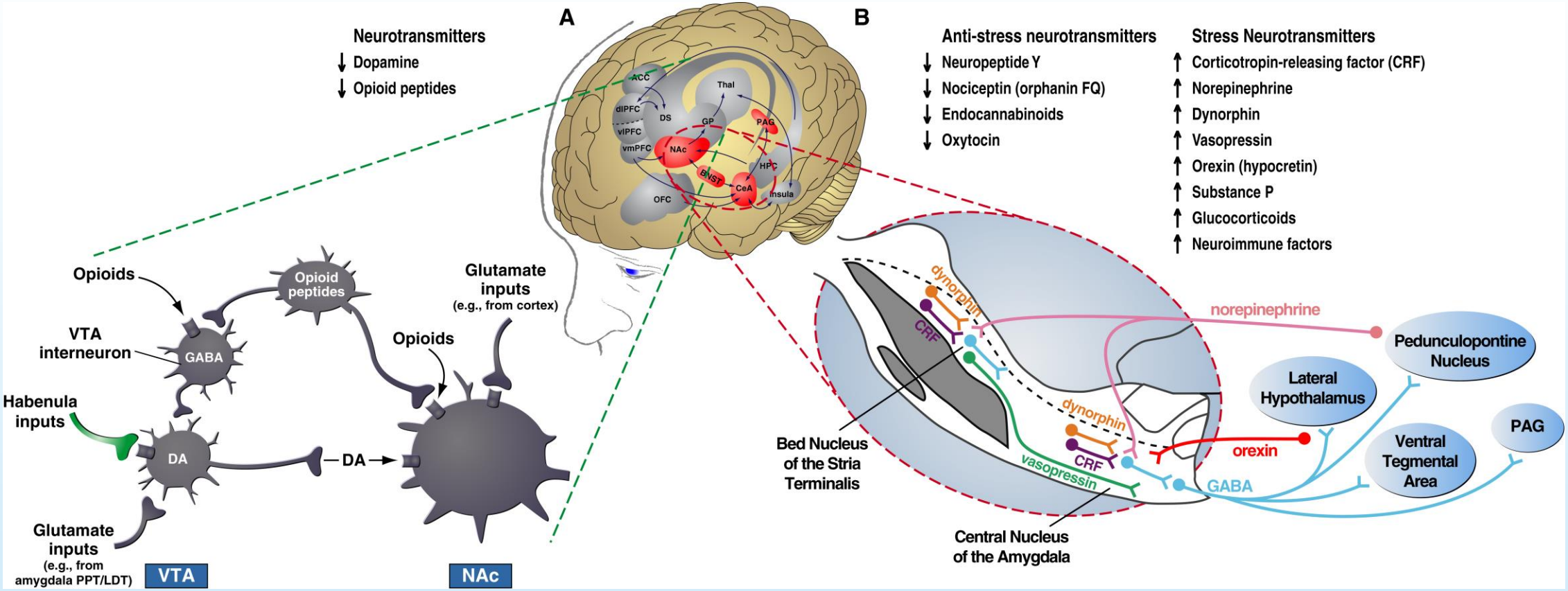
Rebound, drug opposite effects including pain
Increases in negative emotional states
Dysphoria
Stress-like symptoms
Decreases in sensitivity to natural rewards
Social withdrawal

(Decreases in the function of the dopamine component of the reward system. Recruitment of brain stress neurotransmitter such as CRF and dynorphin into extended amygdala and habenula)

Koob & Volkow Lancet Psychiatry 2016, Koob Biological Psychiatry 2019, Ballantyne, Sullivan and Koob Pain 2019

Within-system downregulation of brain reward circuitry

Between-system recruitment of brain stress circuitry



Koob & Bloom 1988, Koob and LeMoal 2008

Between system adaptations

- Circuitry change in which another circuit (ie stress, or anti-reward) is activated by reward circuits
- Chronic opioid administration dysregulates reward and stress systems to lower reward function and increase stress and pain
- PAG is prominent output of extended amygdala to regulate both somatic and emotional pain, mediates hypernegative emotions and negative prediction errors associated with fear

Koob Annu Rev Psychol 2008, Koob Biologcial Psychiatry 2019

Opioid Dependence

No uncontrollable craving or compulsive use

No harmful use that is not medically directed (patient takes opioid exactly as prescribed)

Withdrawal/drug opposite effects: somatic withdrawal symptoms, hyperalgesia, hyperkatefeia, dysphoria

Difficulty tapering, possibly lifelong

Stress-like symptoms

Reward deficiency and social withdrawal

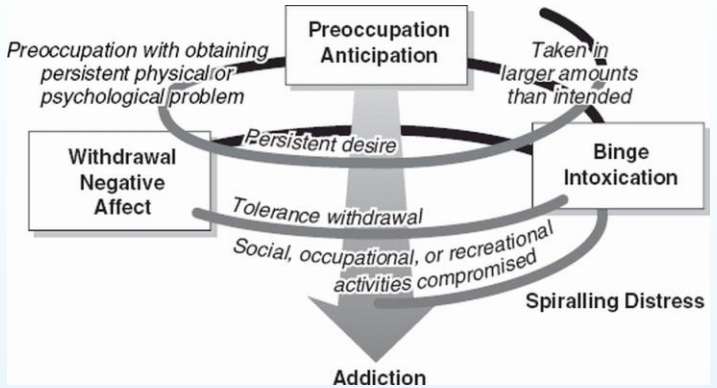
Ballantyne & LaForge, Pain 2007;129:235
Ballantyne et al, Arch Int Med 2012;172:1342
Nestler, Nature Rev Neurosci 2001;2:119
Koob & LeMoal Annu Rev Psychol 2008
Koob & LeMoal 2001
Shurman et al Pain Med 2010
Koob & Volkow Lancet Psychiatry 2016
Ballantyne et al Pain 2019

Francie does not have OUD, but she does have Opioid Dependence

Why not OUD

- Is it fair?
- Is it accurate?
- Does it agree with the neurobiology?

Why this new thinking requires some consideration of old thinking



<u>SOURCES OF CONFUSION</u>

1) The word “physical”

2) DSM IV’s addiction progression ending with “Substance Dependence”

3) That genetic risk is necessary for the development of addiction

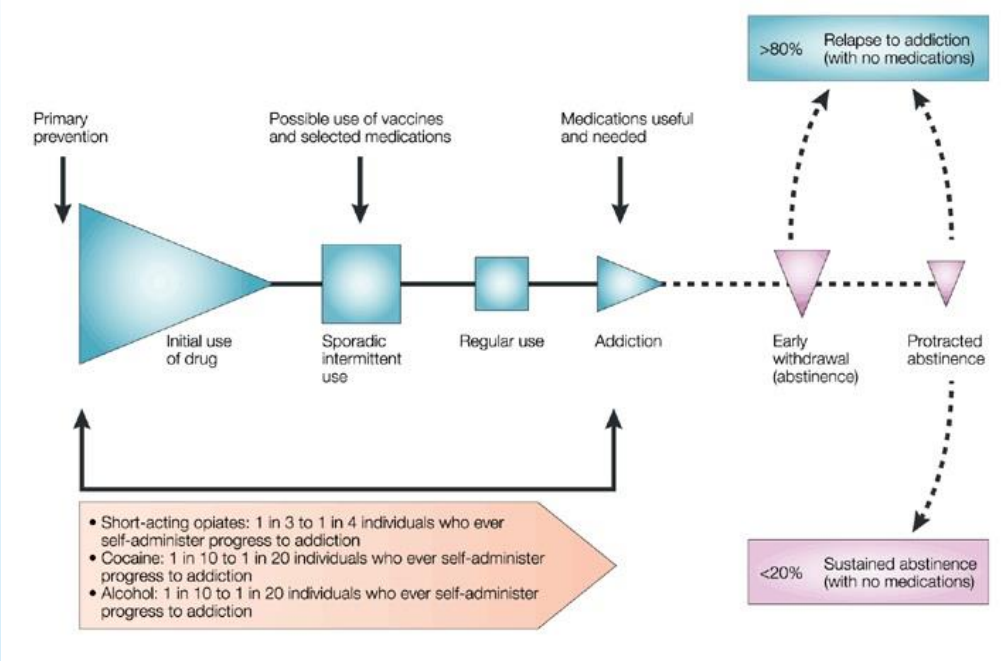
1) The word “physical”

- Understood by different people to mean different things
- In the pain world, the idea is that “physical dependence” consists only of the classical early somatic symptoms of withdrawal
- In the addiction world, “physical” is extended as far as the molecular processes that are consequent to drug use, including psychological changes
- The idea to challenge is that the adaptations will reverse when drug use stops because they were simply the result of drug use

2) DSM IV's addiction progression ending with "Substance Dependence"

- Never fit opioid treated pain patients

- In fact, in pain patients, the progression is the opposite: dependence can develop without compulsive use, or without any of the prior stages of addiction development in DSM IV



Kreek et al Ann NY Acad Sci 2001

3) That genetic risk is necessary for the development of addiction

- TRUE: across a population exposed to a drug, a fairly constant proportion will become addicted (approx. 12% for opioids)

- HOWEVER: Dependence is a risk factor in its own right that will add to genetic risk

- MOREOVER: There are many reasons that people taking opioids continuously for years are more likely to develop addiction than the general population

Kreek et al, Nat Neurosci 2005, Ballantyne et al Pain 2019, Koob Biological Psychiatry 2019

Why Dependence is not Addiction/OUD

Dependence

Continuous withdrawal

Hyper-emotions (hyperkatefeia)

Symptoms of stress

Reward deficiency

Social withdrawal

Addiction/OUD

All of Dependence +

Compulsivity

Lack of control

Defined by behaviors

Laid down as Memory (hard to eradicate)

Chou, Ballantyne, Lembke Annals Int Med 2019 (in press)

Opioid Dependence is distinguished from Opioid Use Disorder to avoid the binary choice between OUD versus no OUD, which is problematic particularly for the many patients who have Opioid Dependence that does not meet criteria for OUD. These patients need treatment akin to OUD treatment BUT, in contrast to OUD:

- It is acceptable to continue the patient's usual opioid (but with supplementary monitoring and support) if attempts to taper result in a deterioration in function and quality of life

- Buprenorphine should be offered specifically to treat Opioid Dependence and pain, and may obviate the need to continue patient's usual opioid

- Where OD and not OUD diagnostic criteria are met, avoidance of the OUD diagnosis relieves the patient from the stigma, employment implications and possible child custody implications of OUD.

Summary

- Dependence is distinct from addiction in that there is no uncontrollable craving or compulsive use
- Reward deficiency (inability to experience natural rewards), negative affect and social isolation accompany established dependence
- Dependence can be hard to reverse
- Dependence can rapidly progress to addiction during withdrawal