# Mood Disorders and Substance Abuse

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The Coalition of Behavioral Health Services

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## True/False:
## All of the following are FDA-approved treatments for alcohol use disorders

- A) disulfiram (Antabuse)
- B) naltrexone
- C) intramuscular injection of naltrexone (Vivitrol)
- D) acamprosate (Campral)
- E) topiramate (Topamax)

- **Answer:** False

**True/False:**

**All of the following are included in the DSM-5 section on depressive disorders:**

- A) specifier, with mixed features
- B) specifier, with anxious distress
- C) melancholia
- D) dysthymia
- E) premenstrual dysphoric disorder

- **Answer:** False

# Objectives

- To review changes in the DSM for mood disorders and addictive disorders
- To understand clinical issues in the dual diagnosis patient
- To discuss clinical cases relevant to dual diagnosis
- To discuss challenges in the clinical management of dual diagnosis patients

# Notable Changes in Depressive Disorders in DSM-5

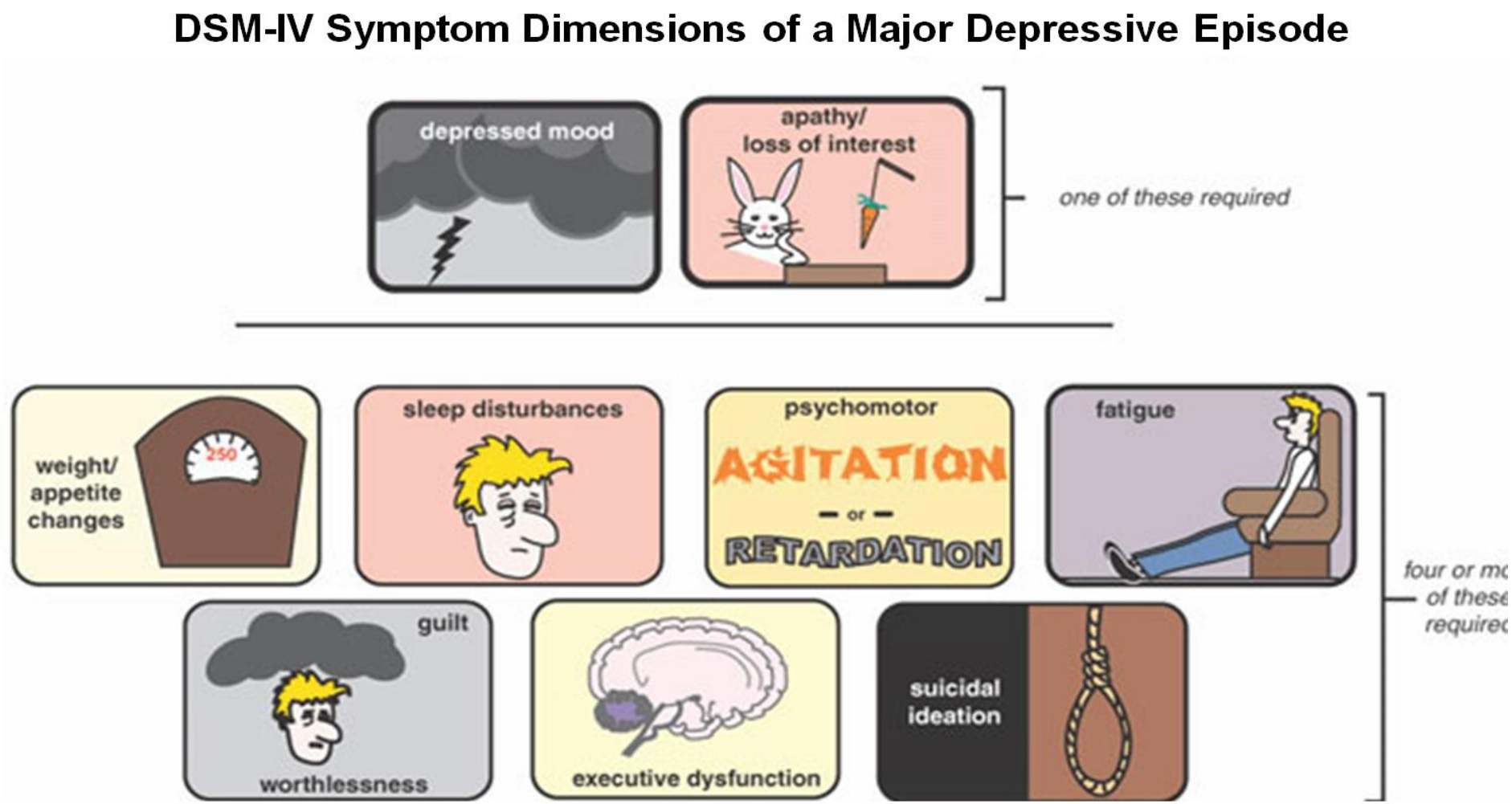
- MDE: elimination of bereavement exclusion

- **Persistent Depressive Disorder** = consolidation of chronic MDD and dysthymia

- NOS Category (DSM-IV) = **Other Specified** or **Unspecified** (DSM-5)
- **Specifiers:**
  - With mixed features
  - With anxious distress
  - With peripartum onset (instead of post-partum)

- Additions:
  - Premenstrual Dysphoric Disorder
  - Disruptive Mood Dysregulation Disorder

# Antidepressants Globally Treat the Following Depressive Symptoms




Stahl SM. *Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Application.* 2013.[2]

# Bereavement in the DSM-5

- Elimination of the “bereavement exclusion” in the diagnosis of MDD

- Rationale:
  - evidence does not support the separation of loss of a loved one from other stressors in terms of its likelihood of precipitating a major depressive episode or the relative likelihood that the symptoms will remit spontaneously

# Specifier: “With anxious distress”

- At least two of the following symptoms during the majority of days of a major depressive episode (MDE):
  - Feeling keyed up or tense
  - Feeling unusually restless
  - Difficulty concentrating because of worry
  - Fear that something awful may happen
  - Feeling that the individual might lose control of himself or herself

  *Specify* current severity:

  **mild**: 2 symptoms; **moderate**: 3 symptoms.

  **moderate-severe**: 4 or 5 symptoms

  **severe**: 4 or 5 symptoms and with motor agitation

# Specifier: “With mixed features”

- At least three of the following manic/hypomanic symptoms are present nearly every day during the majority of days of a MDE:
  - Elevated, expansive mood
  - Inflated self-esteem or grandiosity
  - More talkative than usual or pressure to keep talking
  - Flight of ideas or subjective experience that thoughts are racing
  - Increase in energy or goal-directed activity
  - Increased or excessive involvement in activity with a high potential for painful consequences
  - Decreased need for sleep

**Mixed symptoms are observable by others and represent a change from the person’s usual behavior.**

# Other Specified Depressive Disorder: Examples

- *Recurrent brief depression*
  - Depressed mood + 4 other symptoms lasting 2-13 days occurring monthly for at least 12 months.
- *Short-duration depressive episodes*
  - 5/9 criteria symptoms for 4-13 days
- *Depressive episode with insufficient symptoms*
  - Depressive mood plus one other symptom with clinically significant distress or impairment.

# Melancholia: Not in DSM-5

- ***Impaired hedonic capacity*** with respect to self, future, and surroundings
  - **Consummatory anhedonia**: reduced ability to experience pleasure
  - **Anticipatory anhedonia**: reduced ability to experience the anticipated pleasures that motivates a person to perform an activity

- Sensitization to the negative aspects of self, future, and surroundings

- ***Manifold psychomotor retardation***
  - Slowing and paucity of thoughts
  - Slowed cognitive processing (serial 7s)
  - Reduced conceptual creativity
  - Subjective memory impairment
  - Subjective loss of concentration
  - Sparse, monotonous, and slowed speech

B. Carroll 2012

# DSM-5: Substance-Related and Addictive Disorders

- Alcohol
- Caffeine
- Cannabis
- Hallucinogens
- Inhalants
- Opioids
- Sedatives
- Hypnotics
- Anxiolytics
- Stimulants
- Tobacco
- other

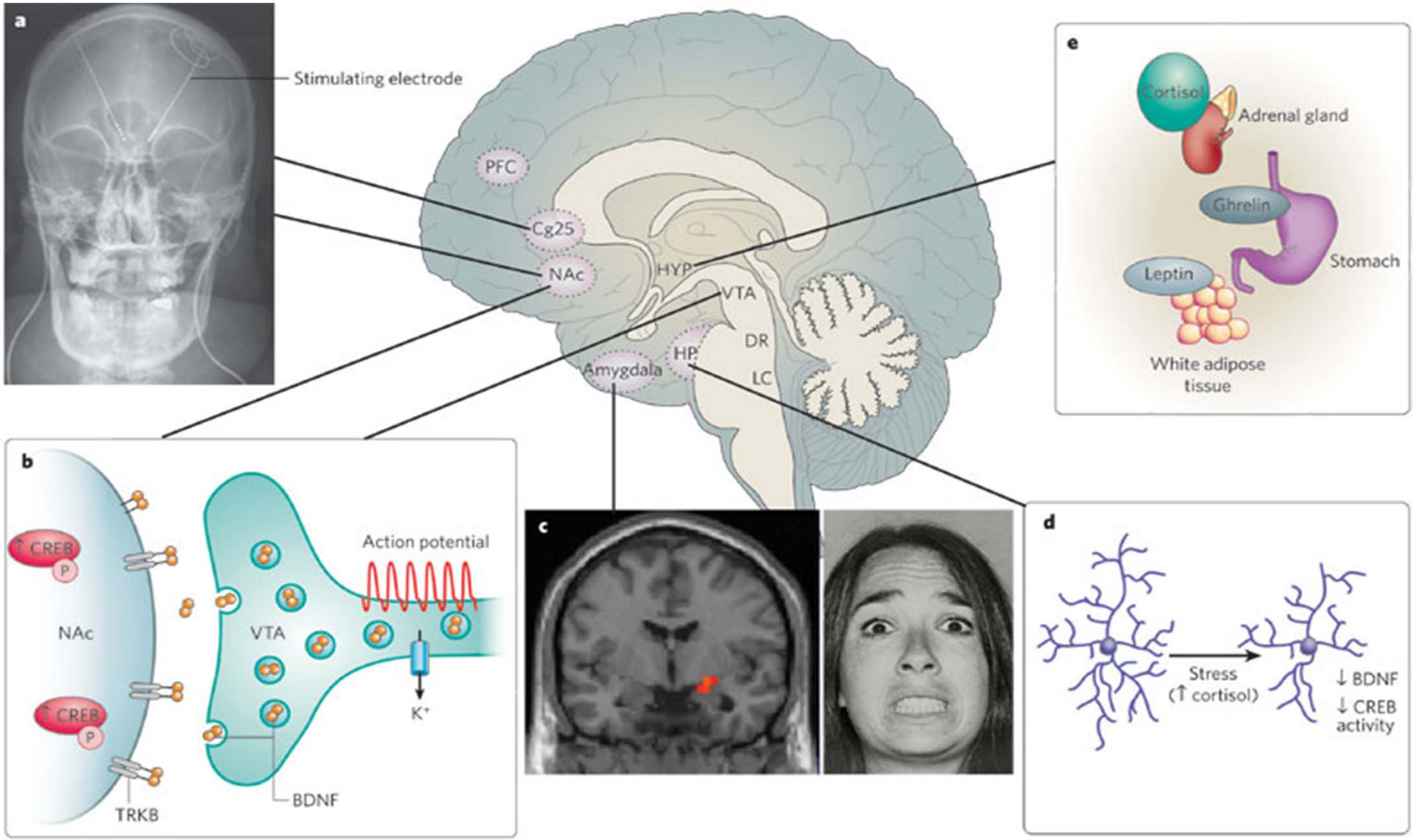
# Addiction vs. Substance Use Disorder

- The term “addiction” is omitted from official DSM-5 substance use disorder terminology
- The term “substance use disorder”
  - More neutral
  - Describes the wide range, from mild form to severe state of chronically relapsing, compulsive drug taking

# Alcohol Use Disorder-DSM-5

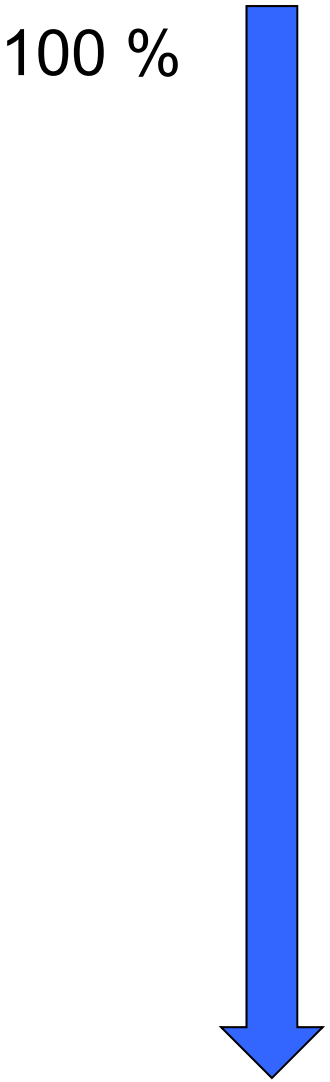
- A problematic pattern of alcohol use leading to clinically significant impairment or distress, with at least 2 of the following, occuring within a 12-month period:
- Coded as mild (2-3), moderate (4-5), or severe (6+)
  - Alcohol taken in larger amounts or over a longer period than intended
  - Persistent desire or unsuccessful efforts to cut down
  - Great deal of time spend in activities necessary to obtain alcohol
  - Craving, or strong desire or urge to use alcohol
  - Failure to fulfill major role obligations
  - Social or interpersonal problems
  - Important social, occupational, or recreational activities given up
  - Recurrent use in situations in which it is physically hazardous
  - Use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused by alcohol
  - Tolerance
  - withdrawal

# The anatomy of melancholy



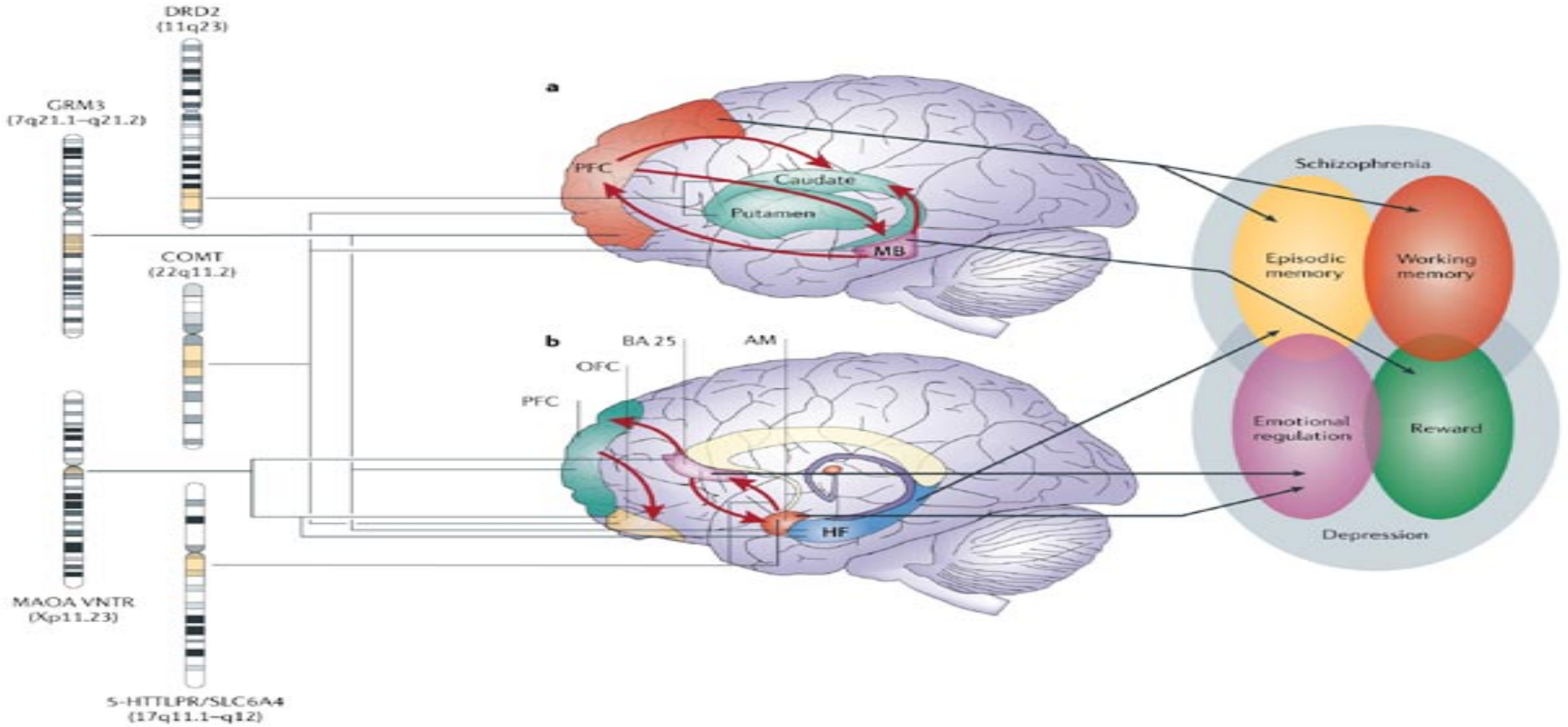

Krishnan & Nestler, 2008

# Psychiatric Disorders and Heritability




- Autism
- ADHD
- Substance dependence: alcohol/heroin/nicotine
- **Bipolar disorder (≈ 70%)**
- Schizophrenia
- Alzheimer's disease
- Obsessive compulsive disorder
- **Anxiety/Unipolar disorders**
- Anorexia
- Substance dependence: THC, Hallucinogens

# Complex path from genes to behavioral and disease phenotype: mediation through brain circuitry






1) **No 1:1 mapping exists between genes and neural system mechanisms, or between mechanisms and behaviour.**
2) **Genes affect neural circuitry→intermediate risk for schizophrenia, depression and various neuropsychological functions**

Meyer-Lindenberg and Weinberger *Nature Reviews Neuroscience* **7**, 818–827 (October 2006) |

# Trial-and-error approach to treatment

**CBT/IPT/Psychodynamic/PST**

**vs.**

Celexa citalopram HBr

Lexapro escitalopram oxalate Well-tolerated strength

ONCE-DAILY VENLAFAXINE HCl EFFEXOR XR EXTENDED RELEASE CAPSULES


zoloft (sertraline HCl)

PAXIL PAROXETINE HCl

Wellbutrin SR (bupropion HCl) SUSTAINED-RELEASE TABLETS 100mg/150mg

# Challenges to Pharmacogenetic Approaches in Psychiatry

- Psychiatric disorders are complex genetic disorders that likely exhibit **Epistasis** (gene-gene interactions) and **epigenetic mechanisms** (e.g. histone modification and DNA methylation, modifiable by environmental factors)
- Non-genetic heterogeneity in drug response (e.g., age, smoking, compliance)
- Phenotype definition
  - Drug-induced side effects
    - patients may be taking multiple medications, comorbidities
    - Underlying illness may contribute to development of adverse event
  - short-term drug response
    - High placebo responsivity
    - Little data on remission rates or relapse prevention

# Epigenetic Mechanisms of Depression

- Key mechanism through which environmental exposures interact with a individual's genetic constitution to determine risk for depression throughout life

- heritable phenotype not coded by a change in DNA sequence (not detectable by genotyping)

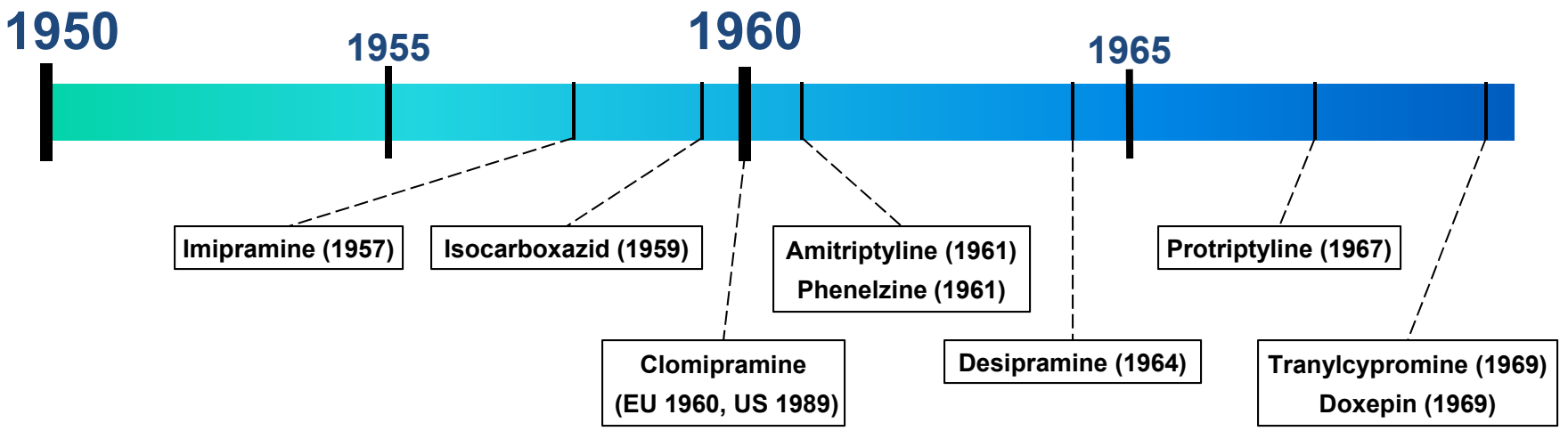
- May modify DNA directly (e.g., **DNA methylation**), alter histones (e.g. **histone acetylation or methylation**) or involve noncoding RNAs (**microRNAs**) that regulate gene expression.

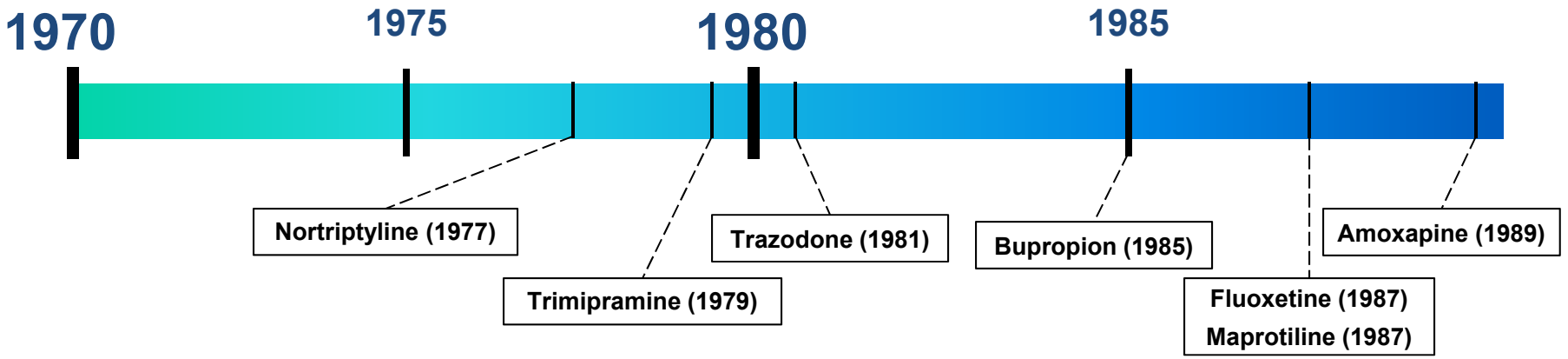
- Epigenetic changes could explain:
  - High discordance rates between monozygotic twins
  - Chronic relapsing nature of disorders
  - Male: female differences in prevalence
  - Largely inconsistent genetic association studies and pharmacogenetic studies

Nestler EJ, *JAMA Psychiatry* 2014

Baylor College of Medicine

# Evolution of Antidepressants: 1950-80s



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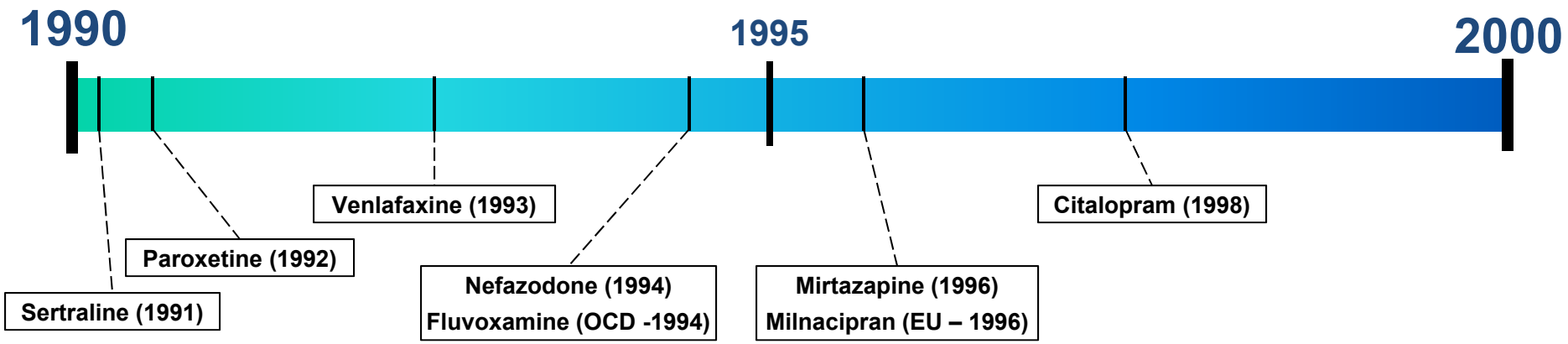
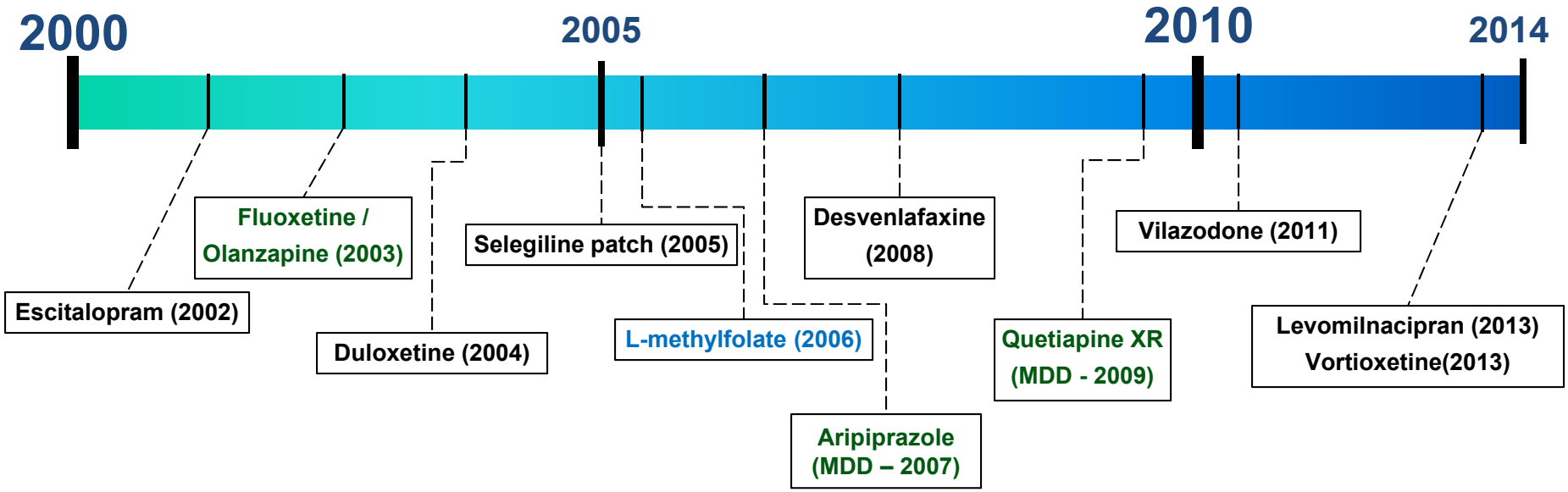
# 1990s - 2014



# Treatment-Resistant Depression

- Not a well-validated diagnosis; no consensus to reliably classify
- FDA definition: When at least 2 adequate antidepressant trials (usually from 2 different pharmacologic classes) fail to produce significant improvement
- TRD affects 20–30% of patients with depression
- 40% of MDD-associated costs are attributed to treatment resistance

Keitner, GI, Mansfield AK, *Psychiatr Clin North Am* 2012

# Risk Factors for Treatment-Resistant Depression

- Anxiety and personality disorder comorbidity
- Early age of symptom onset
- Recurrent episodes
- Nonresponse to the first antidepressant ever tried
- Suicidality
- Melancholic features
- Concurrent medical conditions
- Other factors: history of early life stress and substance abuse

Keitner, GI, Mansfield AK, *Psychiatr Clin North Am* 2012