Wisconsin Public Psychiatry Network Teleconference (WPPNT)

- This teleconference is brought to you by the Wisconsin Department of Health Services (DHS), Division of Care and Treatment Services, Bureau of Prevention Treatment and Recovery and the University of Wisconsin-Madison, Department of Psychiatry.

- Use of information contained in this presentation may require express authority from a third party.

-

WPPNT Reminders

How to join the Zoom webinar

- **Online:** https://dhswi.zoomgov.com/j/1606358142
- **Phone:** 669-254-5252
- Enter the Webinar ID: 160 635 8142#.
  - Press # again to join. (There is no participant ID)

Reminders for participants

- Join online or by phone by 11 a.m. Central and wait for the host to start the webinar. Your camera and audio/microphone are disabled.
- Download or view the presentation materials. The evaluation survey opens at 11:59 a.m. the day of the presentation.
- Ask questions to the presenter(s) in the Zoom Q&A window. Each presenter will decide when to address questions. People who join by phone cannot ask questions.
- Use Zoom chat to communicate with the WPPNT coordinator or to share information related to the presentation.

- Participate live to earn continuing education hours (CEHs). Complete the evaluation survey within two weeks of the live presentation and confirmation of your CEH will be returned by email.
- A link to the video recording of the presentation is posted within four business days of the presentation.
- Presentation materials, evaluations, and video recordings are on the WPPNT webpage: https://www.dhs.wisconsin.gov/wppnt/2024.htm

Aaron Owen, MD

The 5Ws of Antidepressants

Aaron Owen, MD

Clinical Assistant Professor
University of Wisconsin
Department of Psychiatry

- Please be active in the Chat and Q&A!
- Please respond to the polls!
- I'll respond as we go and reserve time at the end for a robust discussion

Who?

What?

Where?

When?

Why?

*Leave the how to the pill pushers like me


Who?

How many people know someone taking an “antidepressant”?

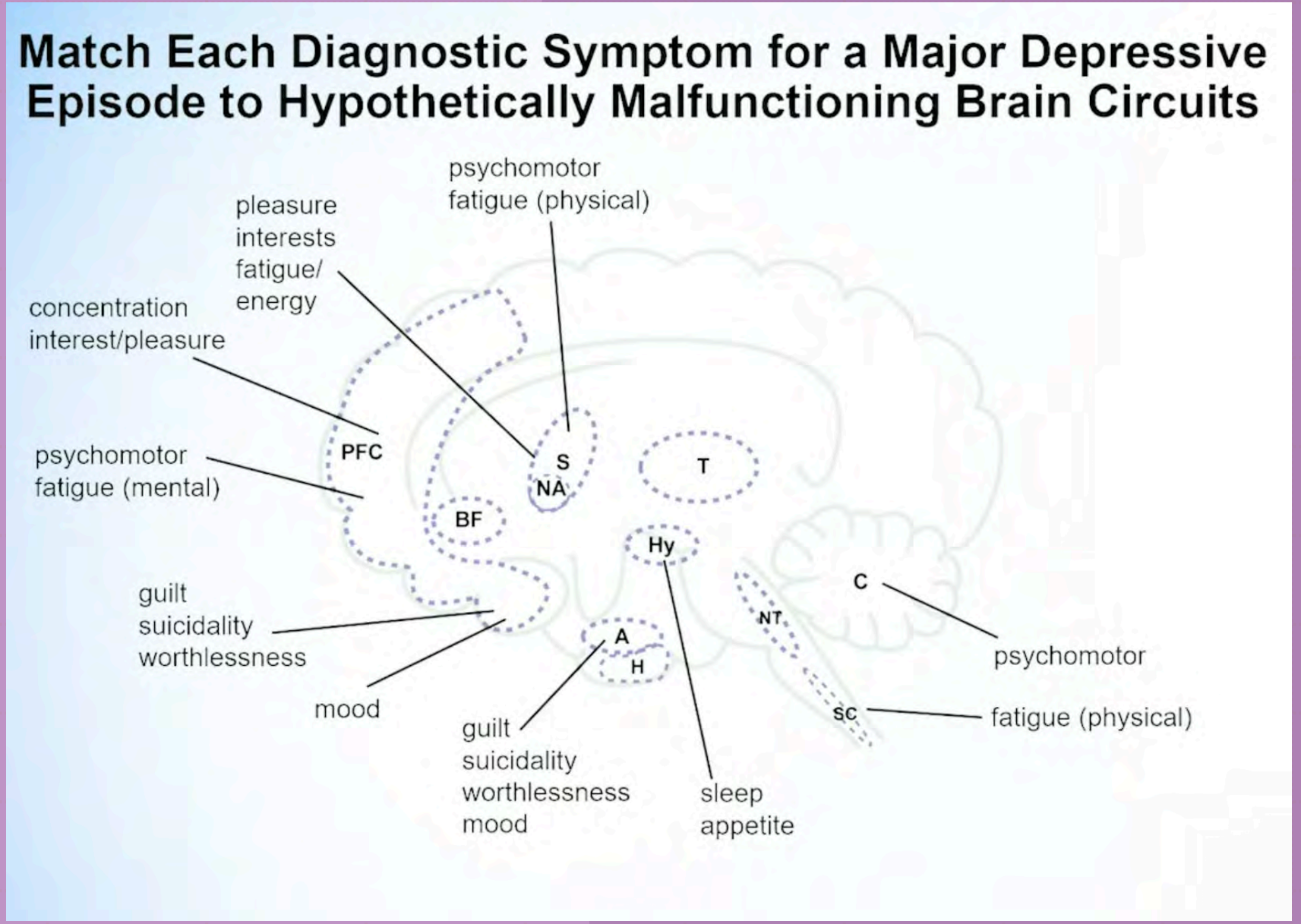
Who?

Looking for people with neurobiological treatment targets (as opposed to exclusively psychosocial)

- Major depressive disorder (MDD)
- ***Clinical Depression*** is a recurrent cognitive/physiologic state, not a transient feeling of sadness or experience of distress.
- It is a *syndrome*, with many combinations of symptoms possible

Target treatment to malfunctioning brain circuit (based on symptoms)

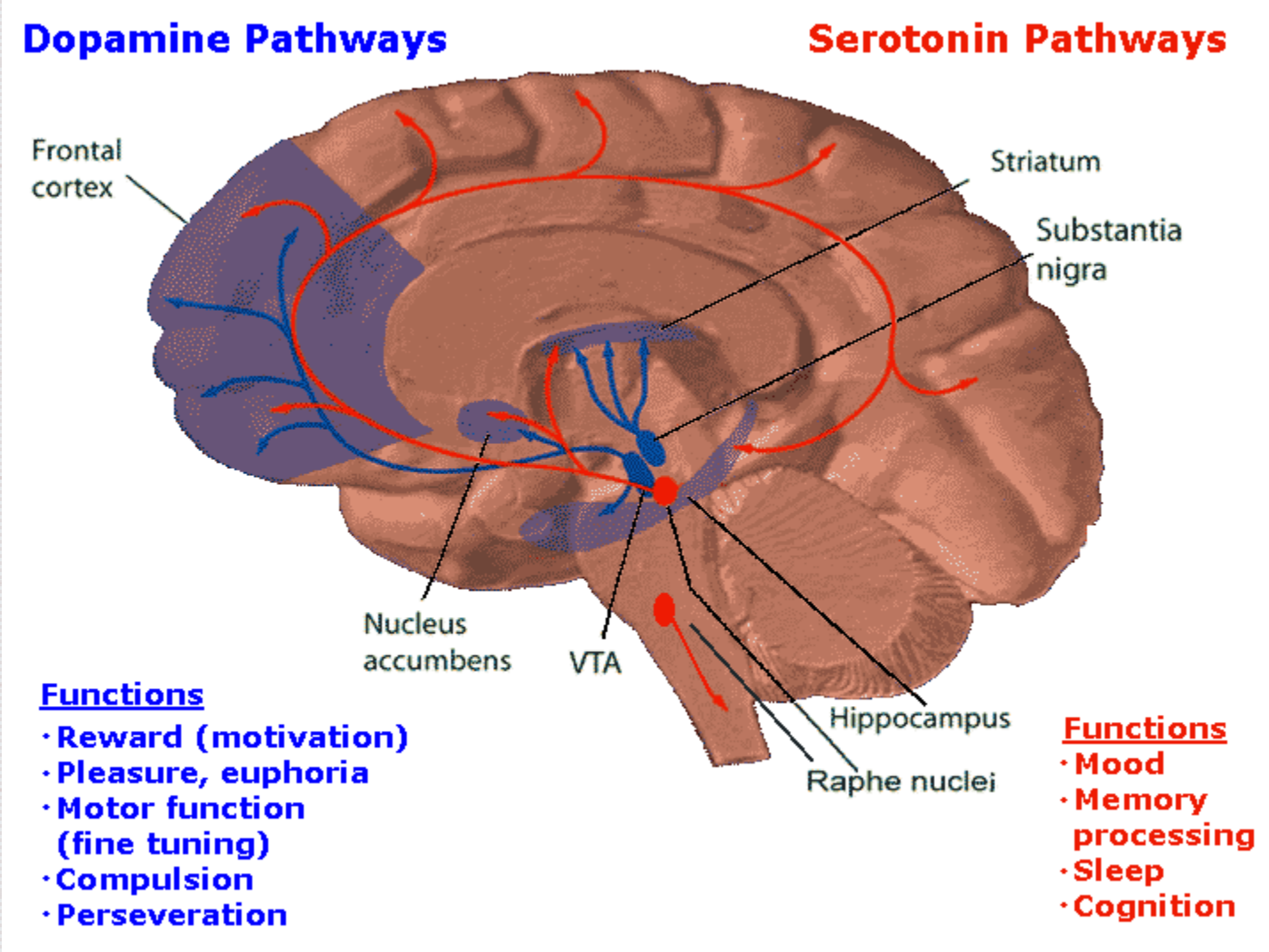
- Psychomotor fatigue: Striatum
- Interest: Ventral Striatum
- Concentration: Prefrontal cortex
- Insomnia: Hypothalamus



Stahl's Essential Psychopharmacology, Chapter 06b: Mood Disorders: Overview and Neurobiology

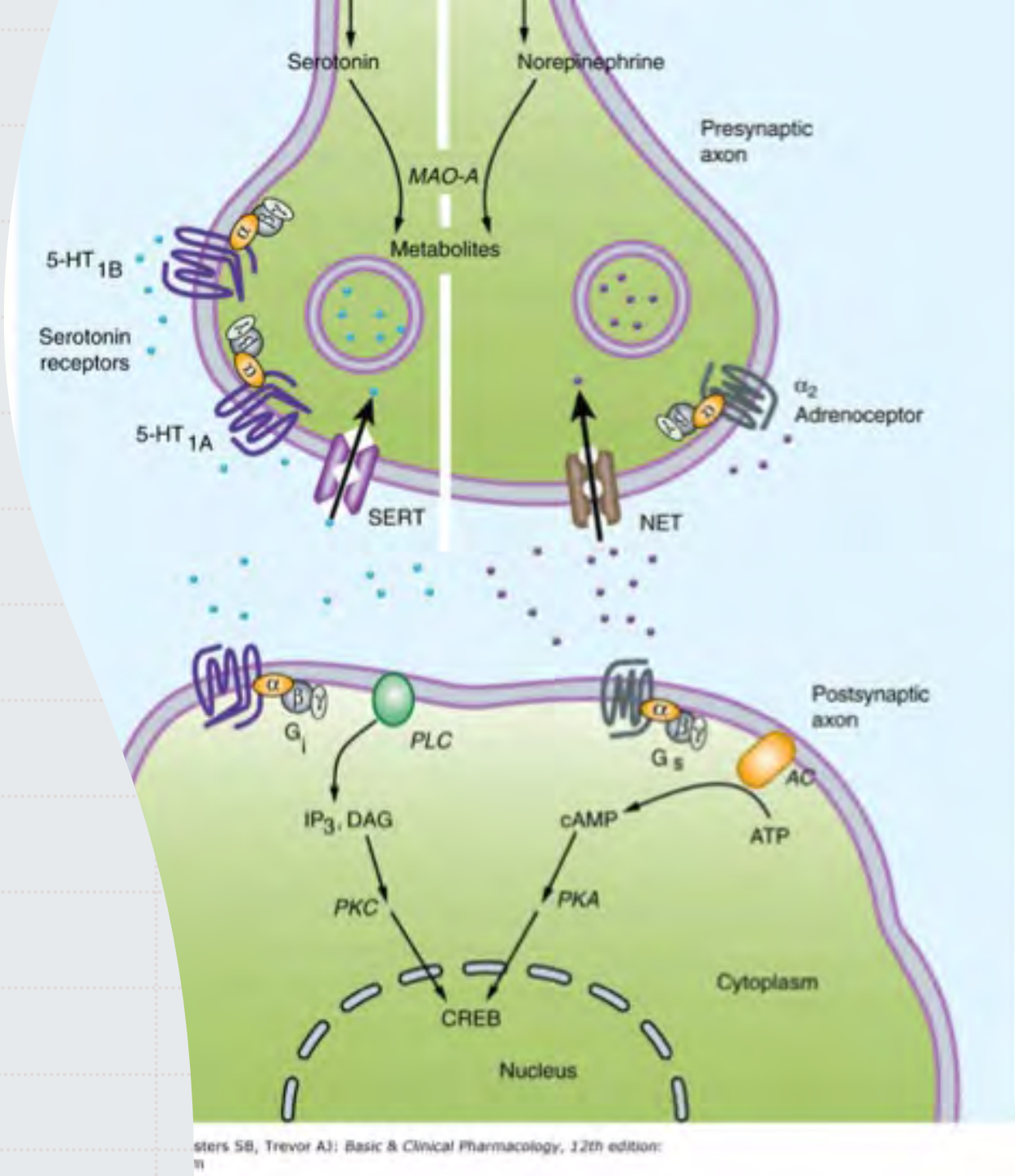
dorsal raphe nucleus

- Produces serotonin
- Responsive to stressors
- Anatomic difference in depression and suicide



Monoamine hypothesis

- Theorized over 70 years ago
- Serotonin, Norepinephrine, Dopamine
- People assumed there was a depletion leading to receptor upregulation
- Drugs boost available neurotransmitters, but there is more to it than this

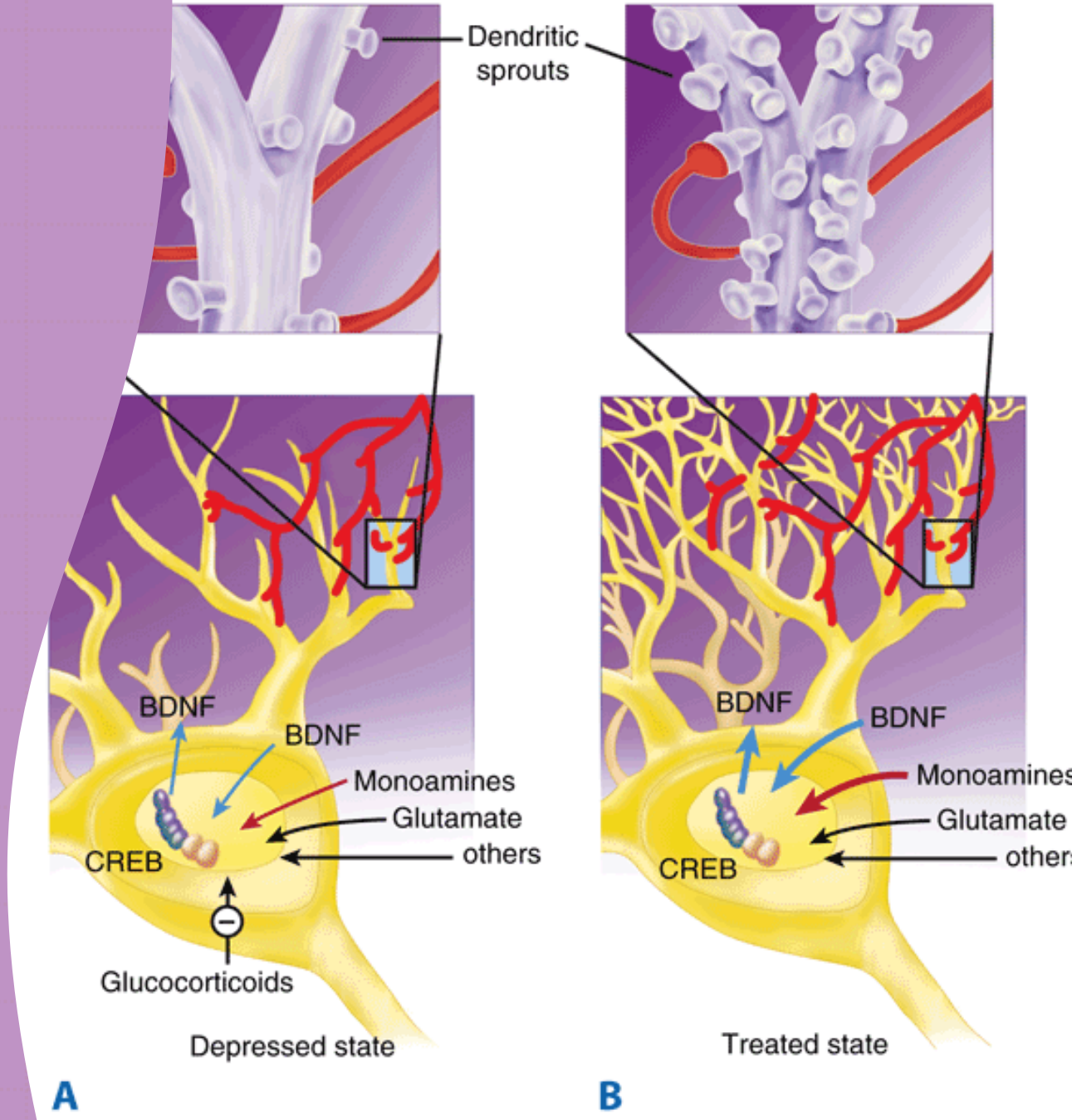


sters SB, Trevor AJ): *Basic & Clinical Pharmacology, 12th edition*:

Neurotrophic Hypothesis

Delayed downregulation of receptors over weeks

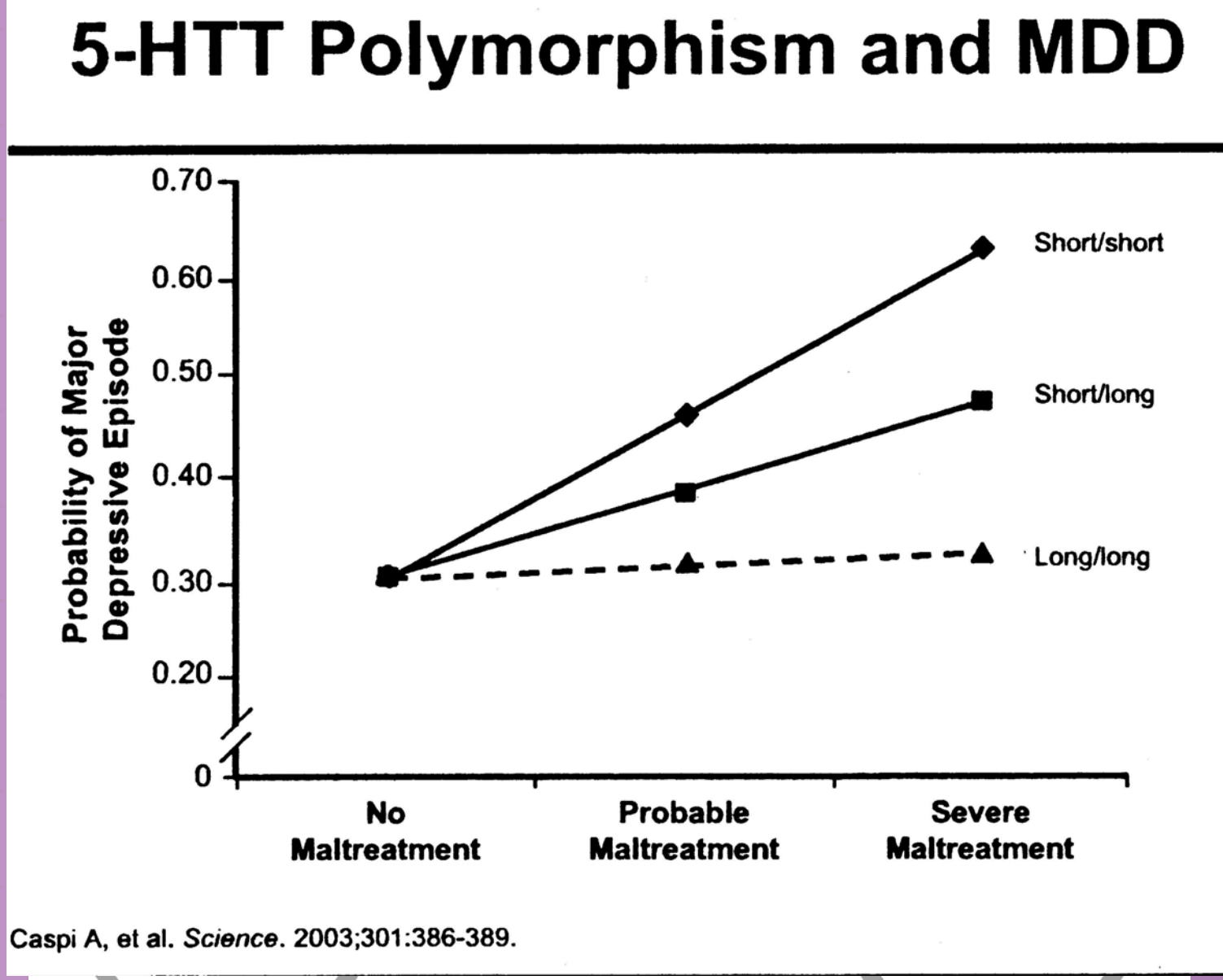
BDNF impacts neuronal growth and survival



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 12th edition*: www.accessmedicine.com

Neuroinflammation

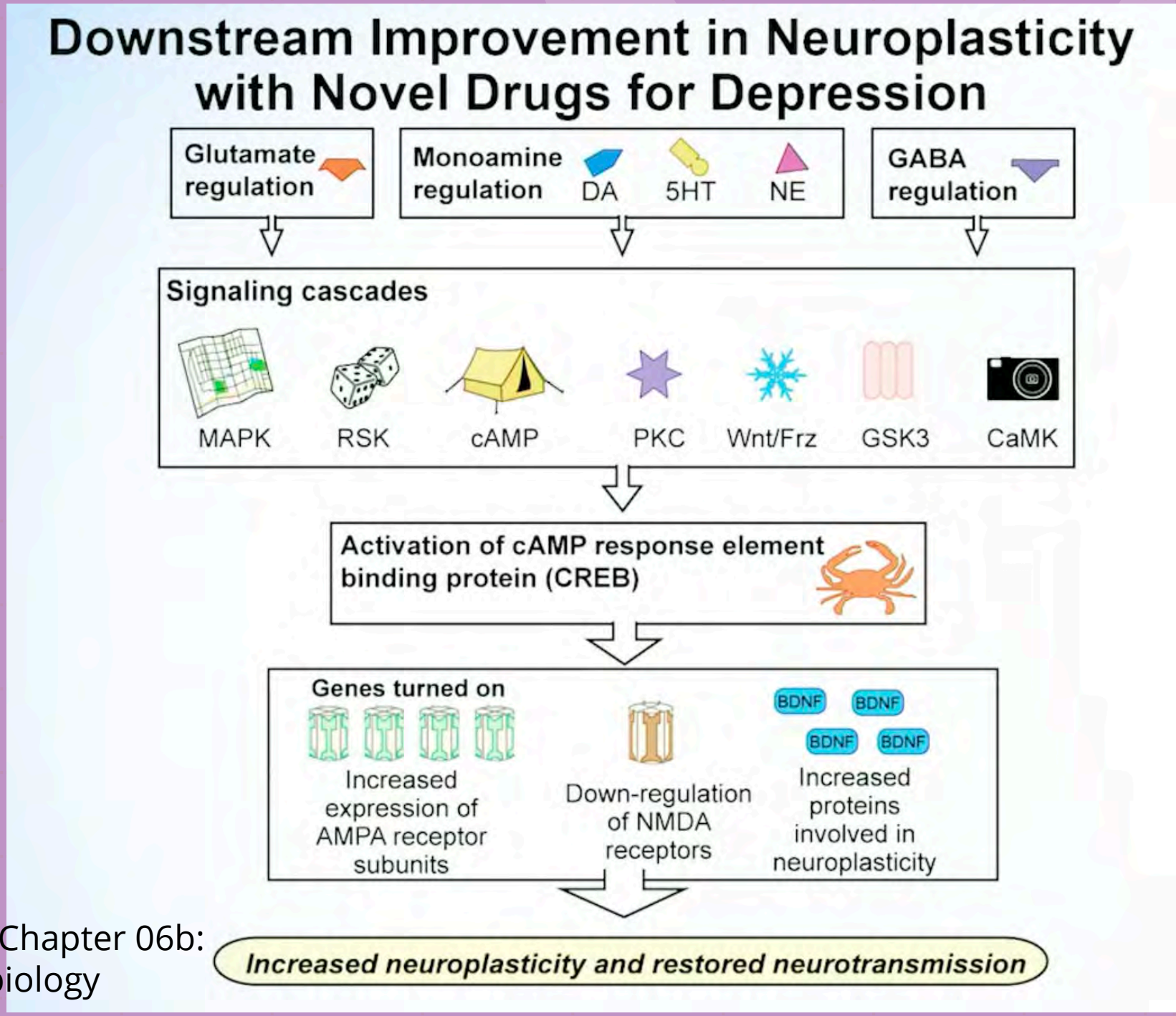
- Stress-induced downregulation of BDNF
- Cytokines released from activated brain microglia can open the blood brain barrier to immune cells that damage synapses/neurons
- So far no drugs targeting this neuroinflammation directly have been successful



El Hage W, Powell JF, Surguladze SA. Vulnerability to depression: what is the role of stress genes in gene × environment interaction? *Psychological Medicine*. 2009;39(9):1407-1411. doi:10.1017/S0033291709005236

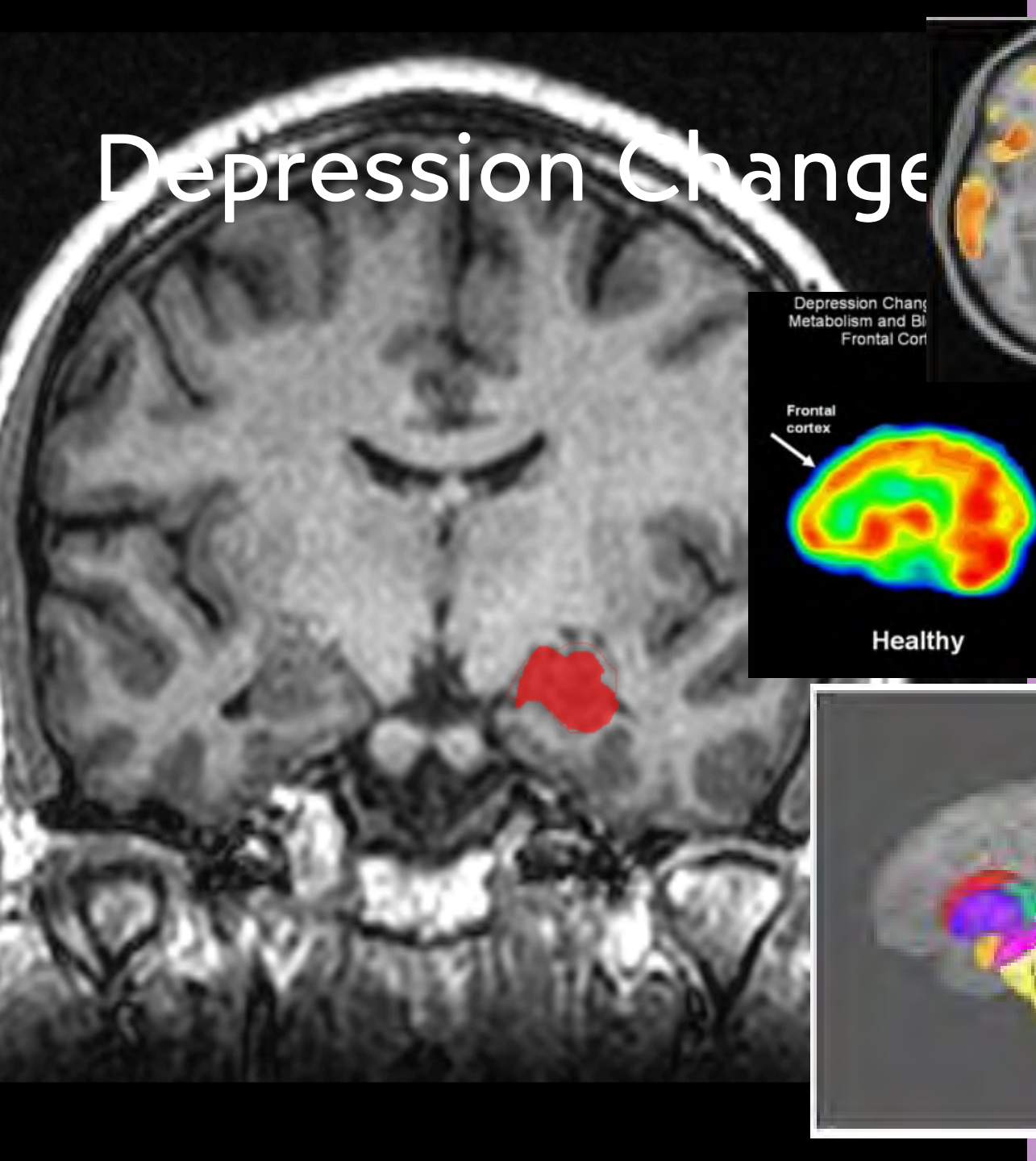
Neuroplasticity Hypothesis of Depression

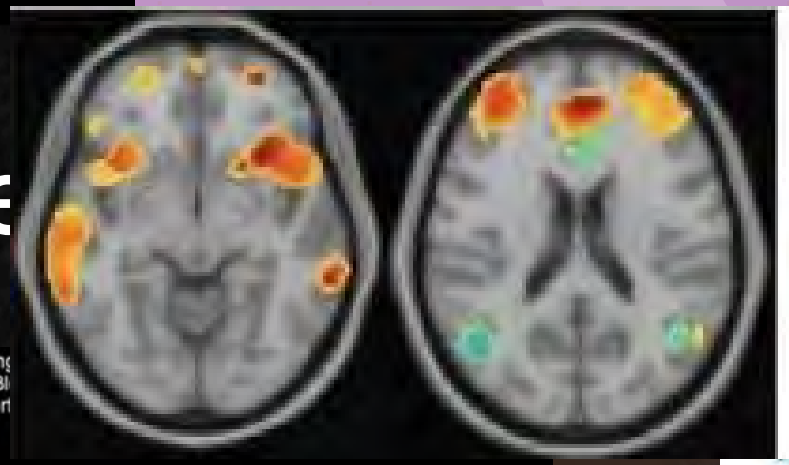
- Goes beyond Monoamines

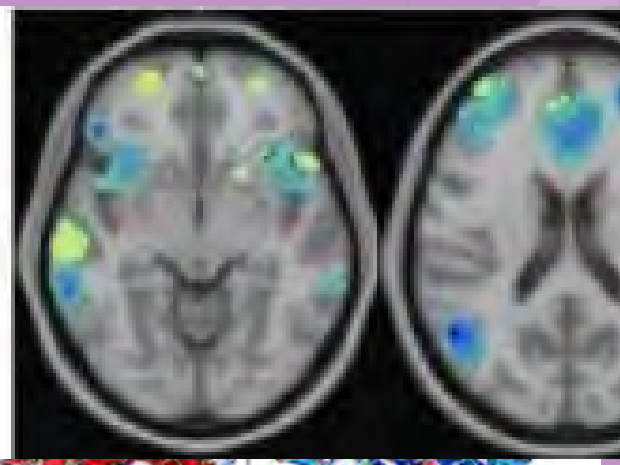


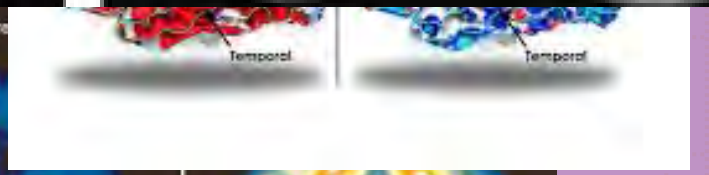
Stahl's Essential Psychopharmacology, Chapter 06b: Mood Disorders: Overview and Neurobiology

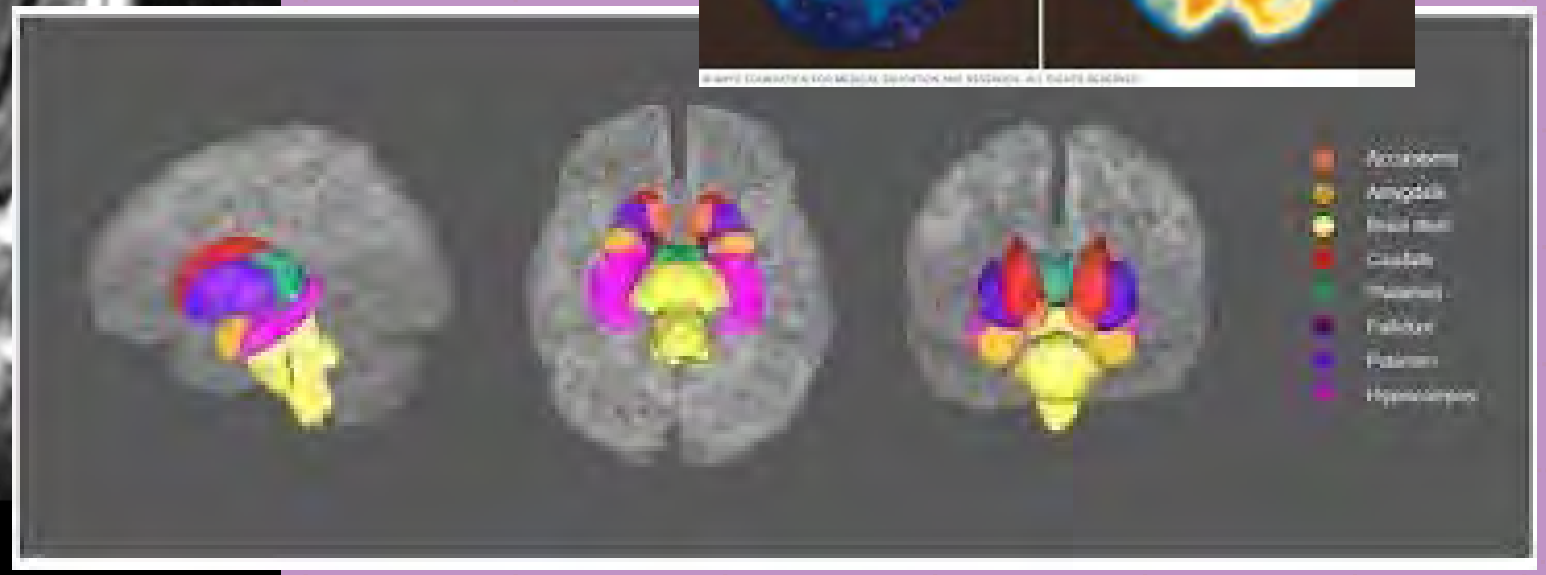
Depression Change











Depression Changes the Brain

- The medications (and other treatments!) for depression target malfunctioning circuits to attempt to restore healthy functioning and prevent chronicity
- For some people with depression, medication might be necessary and sufficient.
- For some people, medication might be necessary and not sufficient.
- For some people, medication isn't necessary.

Other Psychiatric diagnoses

- Generalized Anxiety Disorder
- Panic Disorder
- Obsessive Compulsive Disorder
- Post-traumatic Stress Disorder
- Phobias
- Bulimia
- Adjustment disorder?
- Bipolar depression?

And Medical conditions

- Pain
- Headache
- Perimenopause
- Premature ejaculation


What?

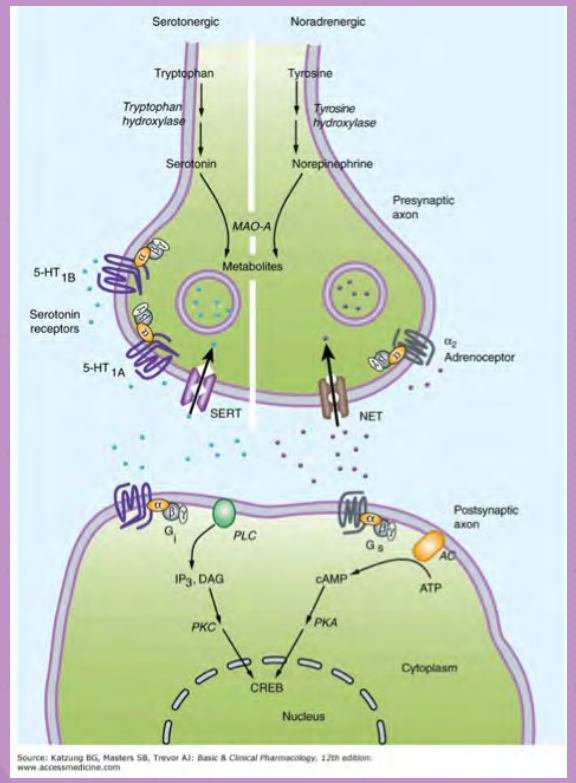
Classical oral antidepressants are thought to modulate which neurotransmitter system?

a) Serotonin
b) Dopamine
c) Norepinephrine
d) GABA

What?

Classic Oral Antidepressants

- SSRI
- SNRI
- MAOi
- TCA
- Atypicals



Honorable Mentions

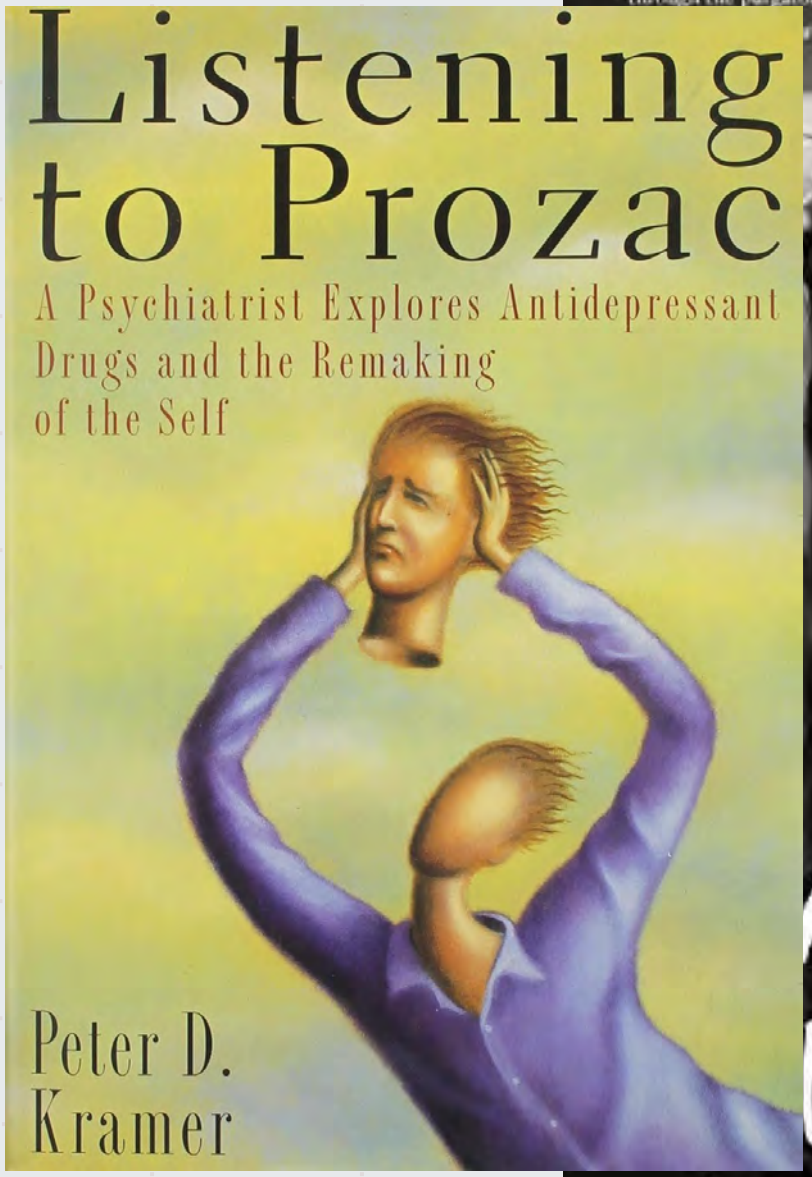
- Mood Stabilizers, SGAs
- Sedatives, stimulants, opioids
- Ketamine, psychedelics
- Thyroid hormone, other hormonal and anti-inflammatory supplements
- TMS, ECT, VNS, Light Therapy

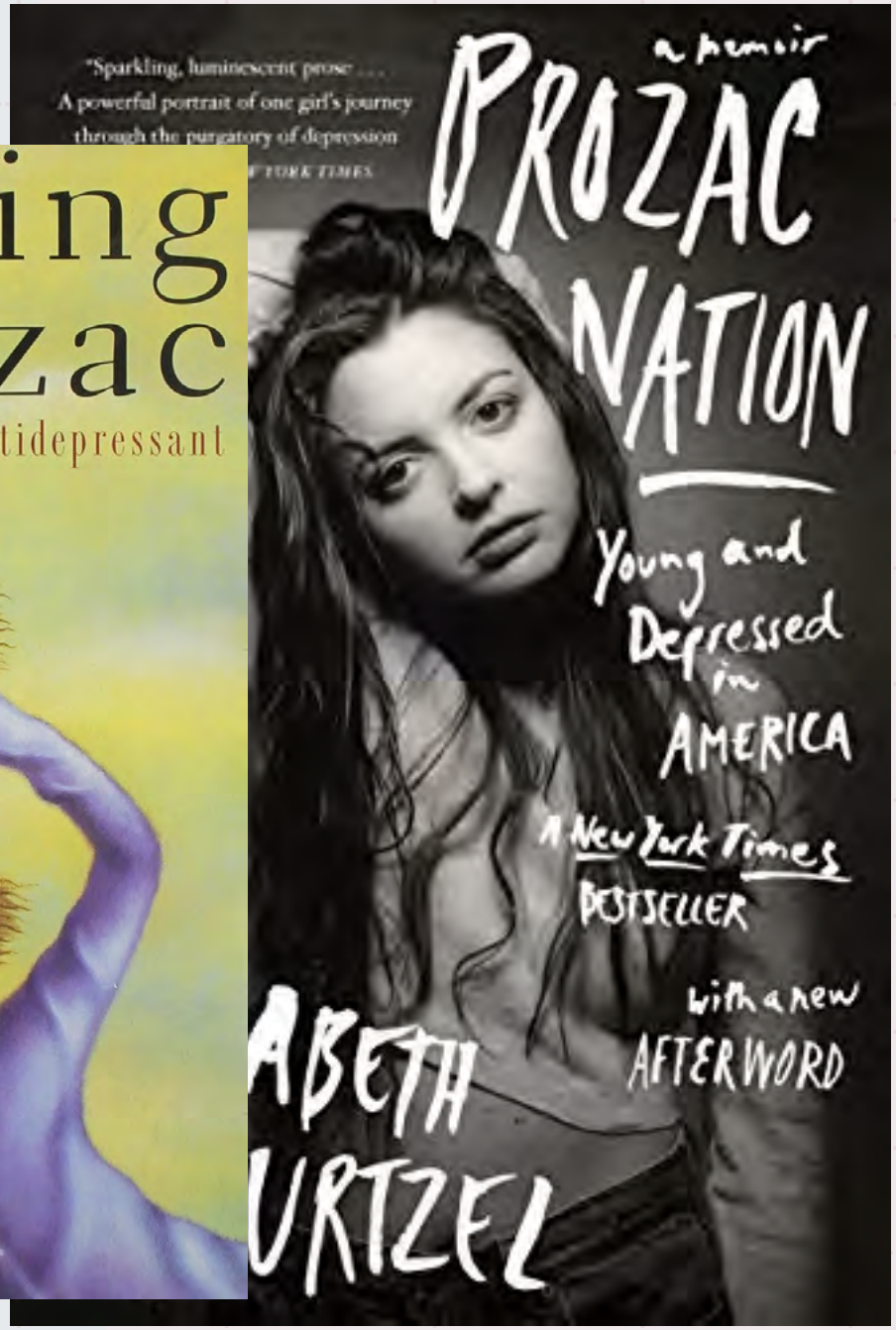
A brief history

- The 1950s saw the clinical introduction of the first two specifically antidepressant drugs: iproniazid, a monoamine-oxidase inhibitor that had been used in the treatment of tuberculosis, and imipramine, the first drug in the tricyclic antidepressant family.
- The first SSRI introduced was fluoxetine (Prozac) in the late 1980s → Prozac Nation

So how did we get from this…

- 1993





To this?

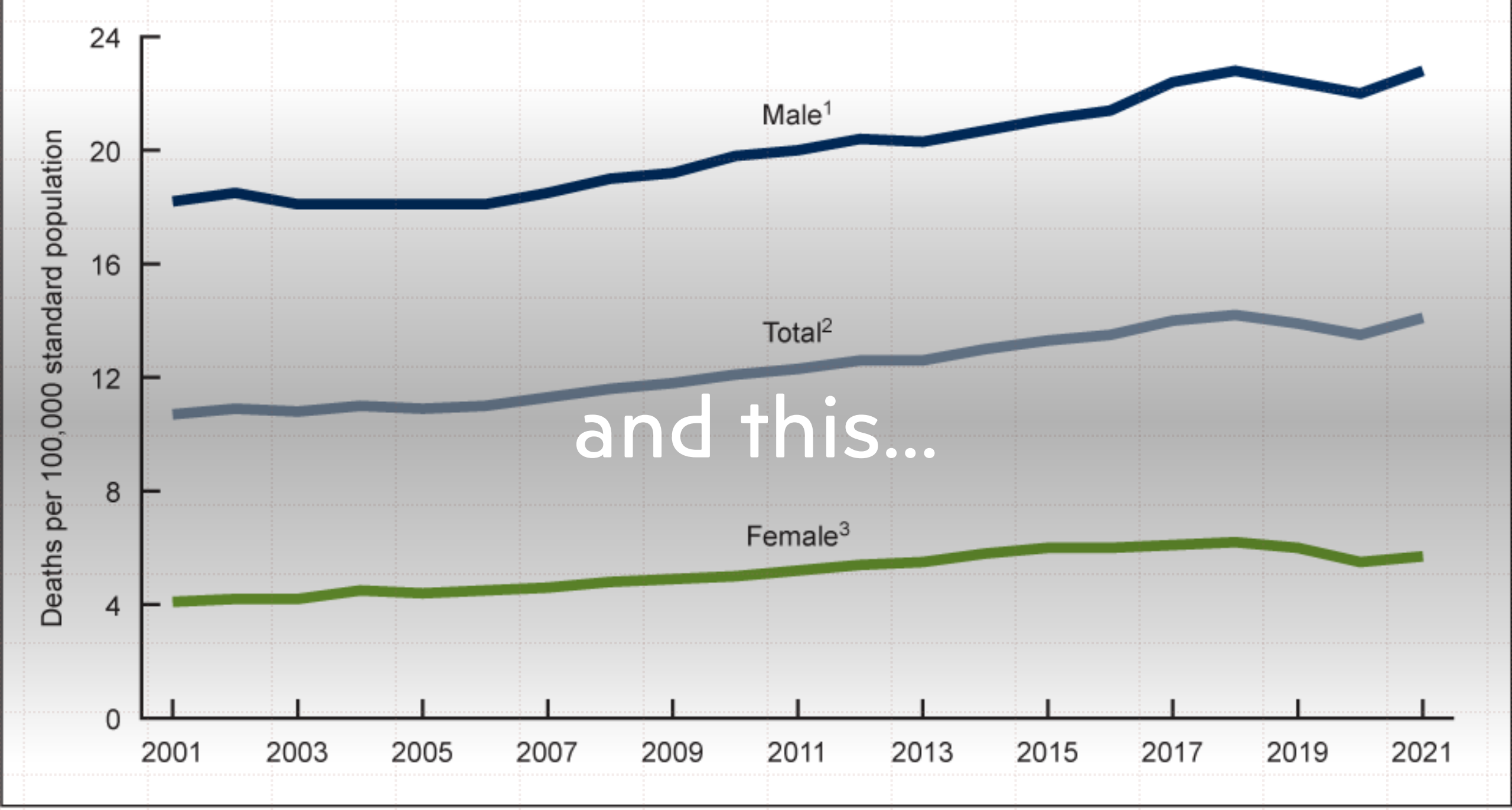
- 2010


ANNA QUINDLEN'S ADVICE FOR AMERICA: LET'S GROW UP, PEOPLE!
FEBRUARY 8, 2010
Newsweek
ANTIDEPRESSANTS DON'T WORK
THE DEBATE OVER THE NATION'S MOST POPULAR PILLS
BY SHARON BEGLEY

To this?

- Even before the emergence of Covid, 1 in 8 American adults was taking an antidepressant drug. According to one estimate, that number rose by 18.6 percent during 2020. Zoloft is now the 12th most commonly prescribed medication in the United States.

Express Scripts' prescribing records
https://www.healthgrades.com/right-care/patient-advocate/the-top-50-drugs-prescribed-in-the-united-states
These rankings for the most common prescription drugs come from the ClinCalc DrugStats database. This database estimates prescription drug usage from the annual Medical Expenditure Panel Survey (MEPS)



[1]No statistically significant trend from 2001 through 2006; significant increasing trend from 2006 to 2018; no statistically significant trend from 2018 through 2021,

- So how many of these people were depressed? How many were taking an antidepressant? And for how many people might a medication been helpful or even necessary but not sufficient?

Federal Statistics in October 2011

- National Center for Health Statistics (NCHS): the rate of antidepressant use in this country among teens and adults (people ages 12 and older) increased by almost 400% between 1988–1994 and 2005–2008.
- one in every 10 Americans takes an antidepressant

Pratt LA, Brody DJ, Gu Q. Antidepressant use in persons aged 12 and over: United States, 2005–2008. NCHS data brief, no 76. Hyattsville, MD: National Center for Health Statistics. 2011.

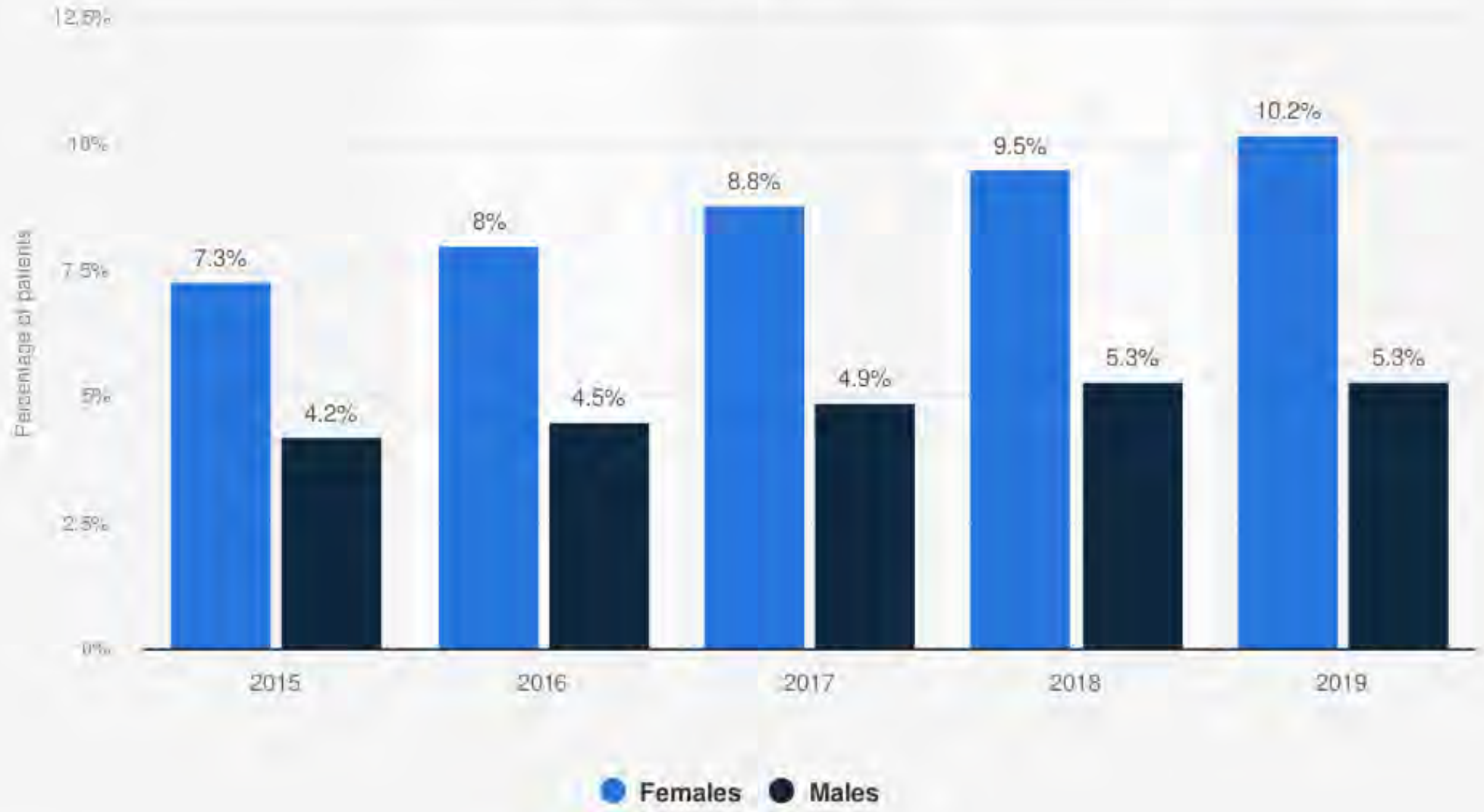
Federal Statistics in October 2011

- 23% of women in their 40s and 50s take antidepressants, a higher percentage than any other group (by age or sex)
- Women are 2½ times more likely to be taking an antidepressant
- 14% of non-Hispanic white people take antidepressants compared with just 4% of non-Hispanic blacks and 3% of Mexican Americans
- Less than a third of Americans who are taking a single antidepressants (as opposed to two or more) have seen a mental health professional in the past year (most from PCP)
- Antidepressant use does not vary by income status.

Federal Statistics in 2018

- During 2015–2018, 13.2% of Americans aged 18 and over reported taking antidepressant medication in the past 30 days.
- Antidepressant use was higher among women than men in every age group. Use increased with age, in both men and women.
- Almost one-quarter of women aged 60 and over (24.3%) took antidepressants

Percentage of teenagers in the United States taking antidepressants from 2015 to 2019, by gender*



Source

Additional Information:

What about the Black Box?

- Prozac (fluoxetine) and Lexapro (escitalopram) are the only **FDA-approved medicines** for teens with **depression**.
- * Black box warning; but claim that increases in child suicide coincided with decreased antidepressant prescribing has been refuted.

- Wheeler, BW, Metcalfe, C, Martin, RM, Gunnell, D. International impacts of regulatory action to limit antidepressant prescribing on rates of suicide in young people. Pharmacoepidemiol Drug Saf 2009; 18: 579–88.

So let’s talk about some specifics...

SSRIs

- **Selective serotonin reuptake inhibitors (SSRIs)**
- SSRIs are the most widely prescribed type of antidepressants. They're usually preferred over other antidepressants, as they cause fewer side effects. An overdose is also less likely to be fatal.
- Fluoxetine is probably the best known SSRI (brand name Prozac)
- Others include citalopram (Celexa), escitalopram (Lexapro), paroxetine (Paxil), sertraline (Zoloft), fluvoxamine (Luvox)

SSRIs: Relatively Selective, Not Completely Selective

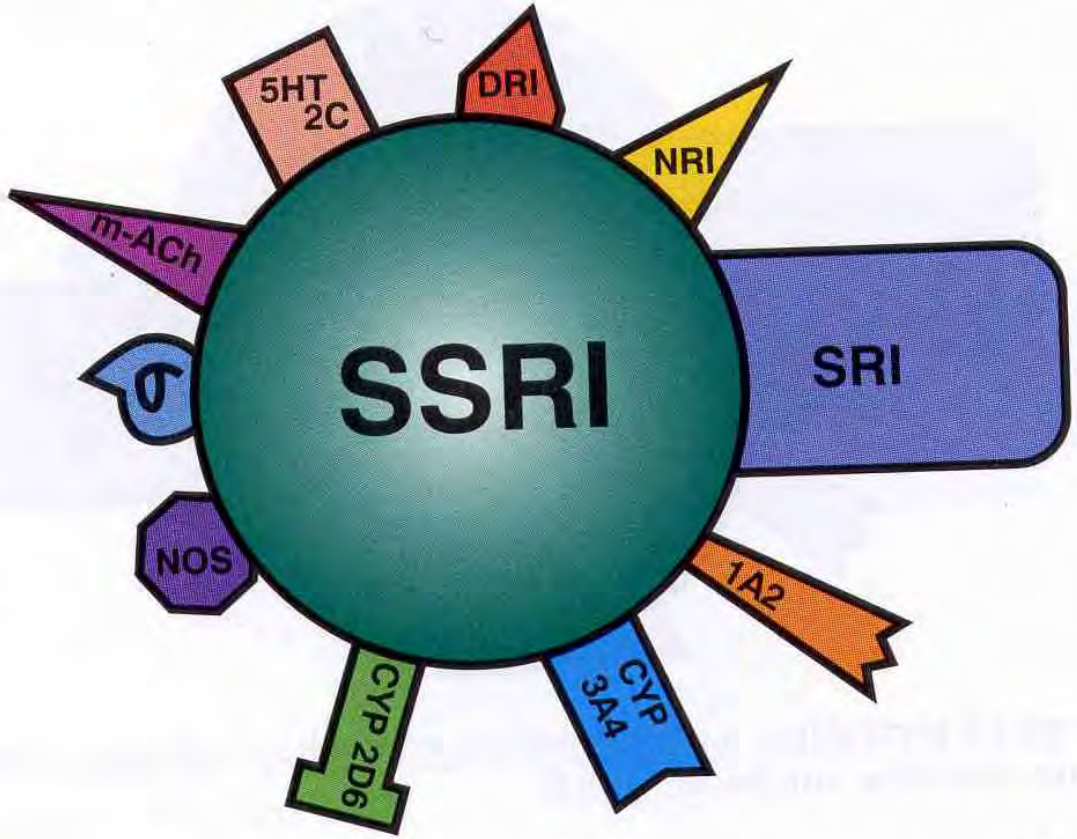


FIGURE 6–40. Icon of various **secondary pharmacologic properties** that may be associated with one or more of the five different **SSRIs**. This includes not only serotonin reuptake inhibition (SRI), but also lesser degrees of actions at other neurotransmitter receptors and enzymes, including norepinephrine reuptake inhibition (NRI), dopamine reuptake inhibition (DRI), serotonin 2C agonist actions (5HT2C), muscarinic/cholinergic antagonist actions (m-ACH), sigma actions (sigma), and inhibition of nitric oxide synthetase (NOS), CYP450 2D6, 3A4, or 1A2.

Essential Psychopharmacology 2nd Ed Stephen Stahl

Different SSRIs have different receptor bindings

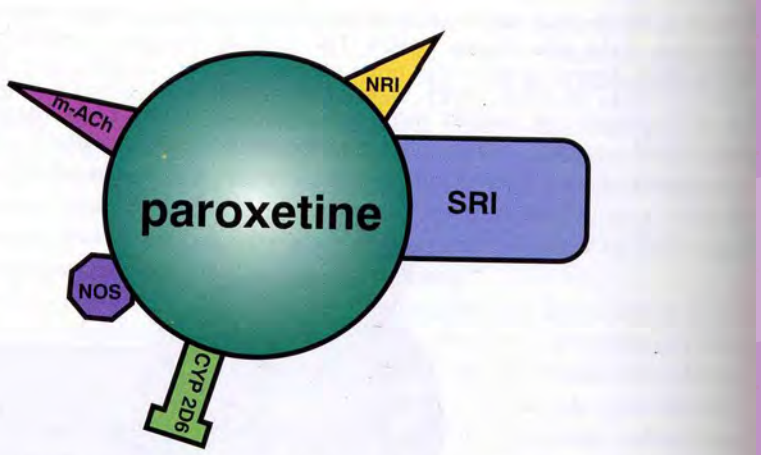


FIGURE 6–43. Icon of **paroxetine** with muscarinic/cholinergic antagonist actions (mACH), norepinephrine reuptake inhibition (NRI), and serotonin 2D6 and 3A4 inhibition, in addition to serotonin reuptake inhibition (SRI).

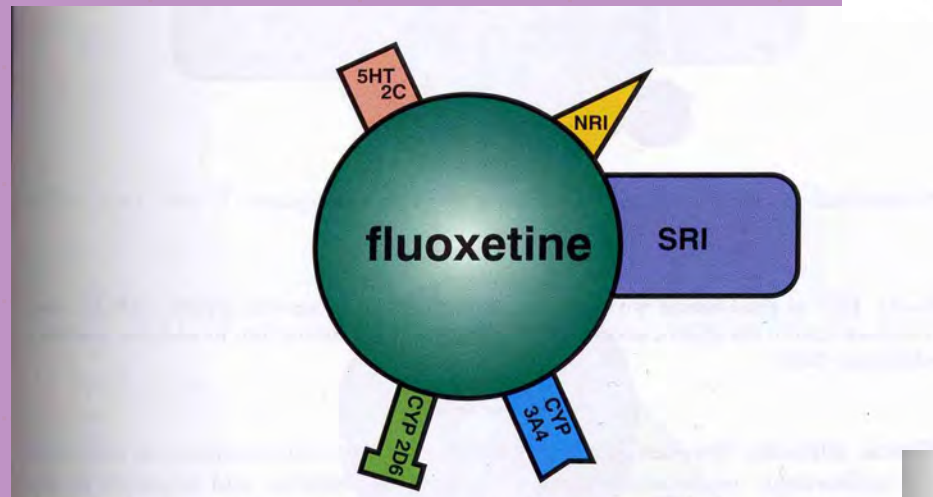
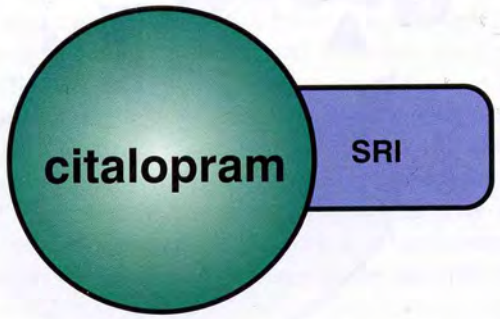


FIGURE 6–41. Icon of **fluoxetine** with serotonin 2C agonist action, norepinephrine re
bition (NRI), and 2D6 and 3A4 inhibition, in addition to serotonin reuptake inhibition



GURE 6–45. Icon of **citalopram**, relatively selective for serotonin reuptake inhibition (SRI).

Essential Psychopharmacology 2nd Ed Stephen Stahl

SSRIs

Clearly work through mechanisms other than just blocking serotonin reuptake

- Time course is too long
- Dose requirement is too high
- Differences in response to different medications

SSRI side effects (generally very safe / very well tolerated)

- Transient but common
  - Headache, nausea
  - Agitation, sleep disturbance, nightmares
  - EPS (extra pyramidal [motor] side effects)
- Excessive Sweating
- Sexual side effects
- Weight gain--more over time
- Drug-Drug interactions
  - More with some SSRIs than others
  - Serotonin syndrome
- Withdrawal syndrome from SSRIs
- Increased tendency to bruise/bleed

Common Reasons for Patient Discontinuation of Antidepressant Medication

Reason	Early Quitter n = 41	Late Quitters n = 28
Did not like side effects	62%	67%
Did not need medication	56%	46%
Felt better	50%	44%
Felt medication not working	32%	52%
Ran out of medication	11%	0%
Doctor said stop taking it	12%	24%
Friend suggested stopping	7%	0%
Gained weight	5%	16%

Adapted from Lin EHB, von Korff M, et al Med Care 1995: 33: 67-74

SNRIs

- **Serotonin-noradrenaline reuptake inhibitors (SNRIs)**
- SNRIs are similar to SSRIs. They were designed to be a more effective antidepressant than SSRIs. However, the evidence that SNRIs are more effective in treating depression is uncertain. It seems that some people respond better to SSRIs, while others respond better to SNRIs.
- Examples of SNRIs include duloxetine (Cymbalta), venlafaxine (Effexor), milnacipran (Savella), and levomilnacipran (Fetzima).

Atypicals

- **Noradrenaline and specific serotonergic antidepressants (NASSAs)**
- NASSAs may be effective for some people who are unable to take SSRIs. The side effects of NASSAs are similar to those of SSRIs, but they're thought to cause fewer sexual problems. Examples include mirtazapine, bupropion, buspirone
- **Serotonin antagonists and reuptake inhibitors (SARIs)**
- SARIs are not usually the first choice of antidepressant, but they may be prescribed if other antidepressants have not worked or have caused side effects (or at low dose for anxiety/insomnia).
- The main SARI prescribed in the US is trazodone

TCAs

- **Tricyclic antidepressants (TCAs)**
- TCAs are an older type of antidepressant. They're no longer usually recommended as the first treatment for depression because they can be more dangerous if an overdose is taken. They also cause more unpleasant side effects than SSRIs and SNRIs.
- Exceptions are sometimes made for people with severe depression that fail to respond to other treatments. TCAs may also be recommended for other mental health conditions, such as OCD and bipolar disorder.
- Examples of TCAs include amitriptyline, clomipramine, dosulepin, imipramine, lofepramine and nortriptyline.
- Some types of TCAs, such as amitriptyline, can also be used to treat chronic nerve pain.

MAOIs

- **Monoamine oxidase inhibitors (MAOIs)**
- MAOIs are an older type of antidepressant that are rarely used nowadays.
- They can cause potentially serious side effects so should only be prescribed by a specialist.
- Examples of MAOIs include tranylcypromine, phenelzine and isocarboxazid.

Recent additions

- Vilazodone (2011) (Viibryd) SSRI and 5 HT1A agonist
- may cause less emotional blunting than typical SSRIs and SNRIs
- REPORTEDLY: no weight gain or sexual dysfunction, no withdrawal effects
- Vortioxetine (2013) (Brintellix) SSRI + HT1A agonist +
- 55% remission rate in treatment resistant pts
- Has been studied in geriatric patients
- May be useful in cognitive deficits of depression (NEJM 2006; 354 1131-42)
- Levomilnacipran (2013) (Fetzima) SNRI

Drawbacks of medications

- All antidepressants can carry side effects, including nausea, weight gain, dizziness, sedation, insomnia, and sexual dysfunction. They usually take several weeks to take effect. Up to a third of people with depression don't respond to these drugs (another third my have only partial response)

Relative Overdose Toxicity

Doxepin	**2.6**
Clomipramine	1.4
Trimipramine	1.7
Imipramine	1.5
Nortriptyline	1.3
Venlafaxine	0.29
Mirtazapine	0.22
Citalopram	0.12
Sertraline	0.05
Fluoxetine	0.03
Paroxetine	0.03

Ratio of fatal/non-fatal overdose relative to amitriptyline

Hawton et al
Brit J Psych
2010; 196
May 354-358

STAR*D

- Federally funded, multi-site
- “Practical” clinical trial, broad inclusion trial
- Equipoise stratified randomization
- Primary outcome = Depression Remission

STAR*D

Level I

- 4000 patients treated with citalopram up to 60 mg/day [remission of 27.5 %]

Level II

- either switch to another antidepressant Bupropion [remission of 21.3 %], sertraline [18.1 %], or venlafaxine [24.4%]

Or

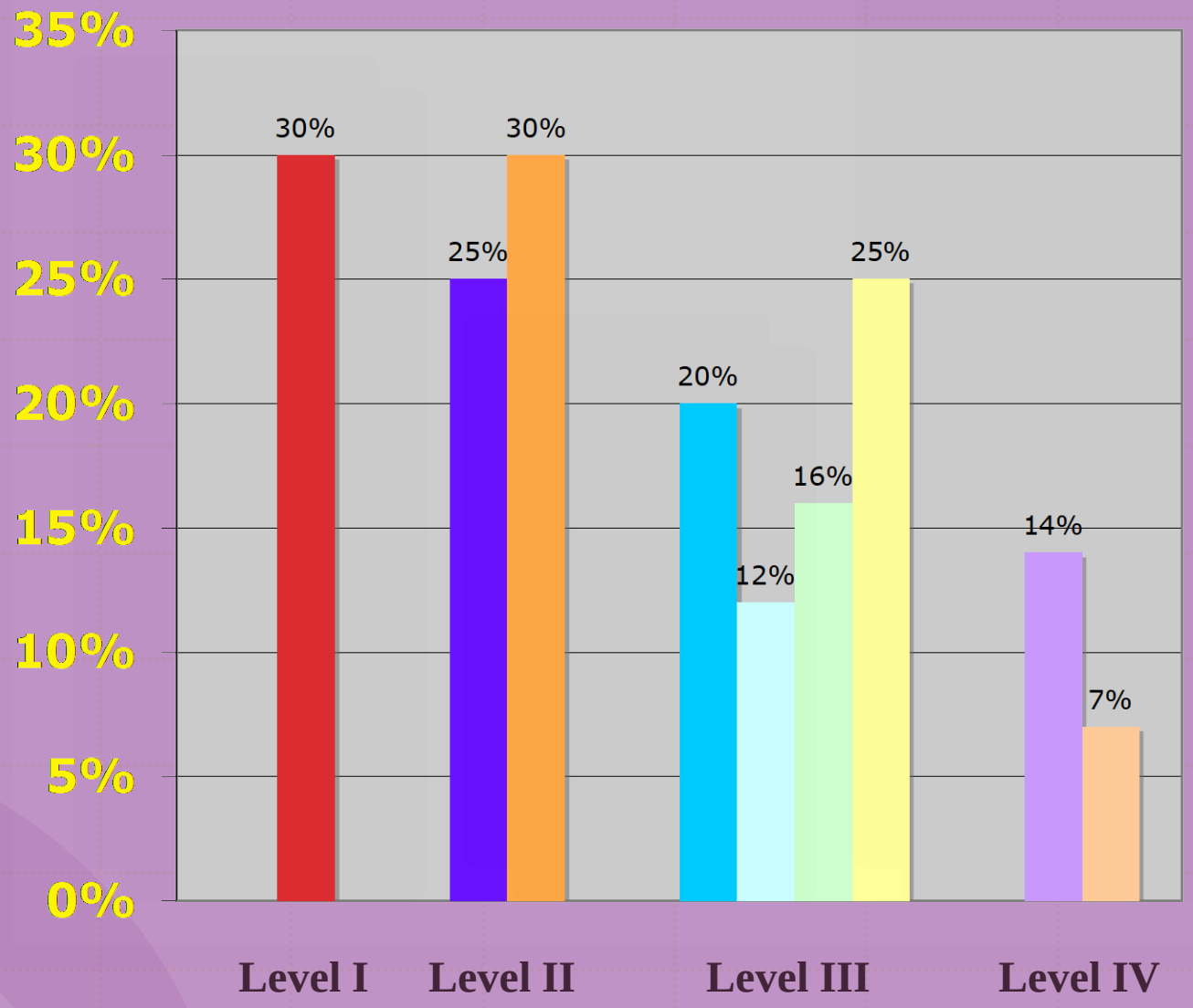
- Augment citalopram with bupropion [29.7%, buspirone 30.2%, or CBT

STAR*D

Level III: randomly assigned to mirtazapine [remission of 12.3 %] or nortriptyline [19.8%]

Level IV: Effexor + mirtazapine or Trancyclopromine

STAR*D Results



Level I

citalopram

Level II

Switch to Bupropioin, Sertraline, Effexor

Augment: Bupropion, Buspiron

Level III

Switch: Nortriptyline

Switch: Mirtazapine

Augment Lithium

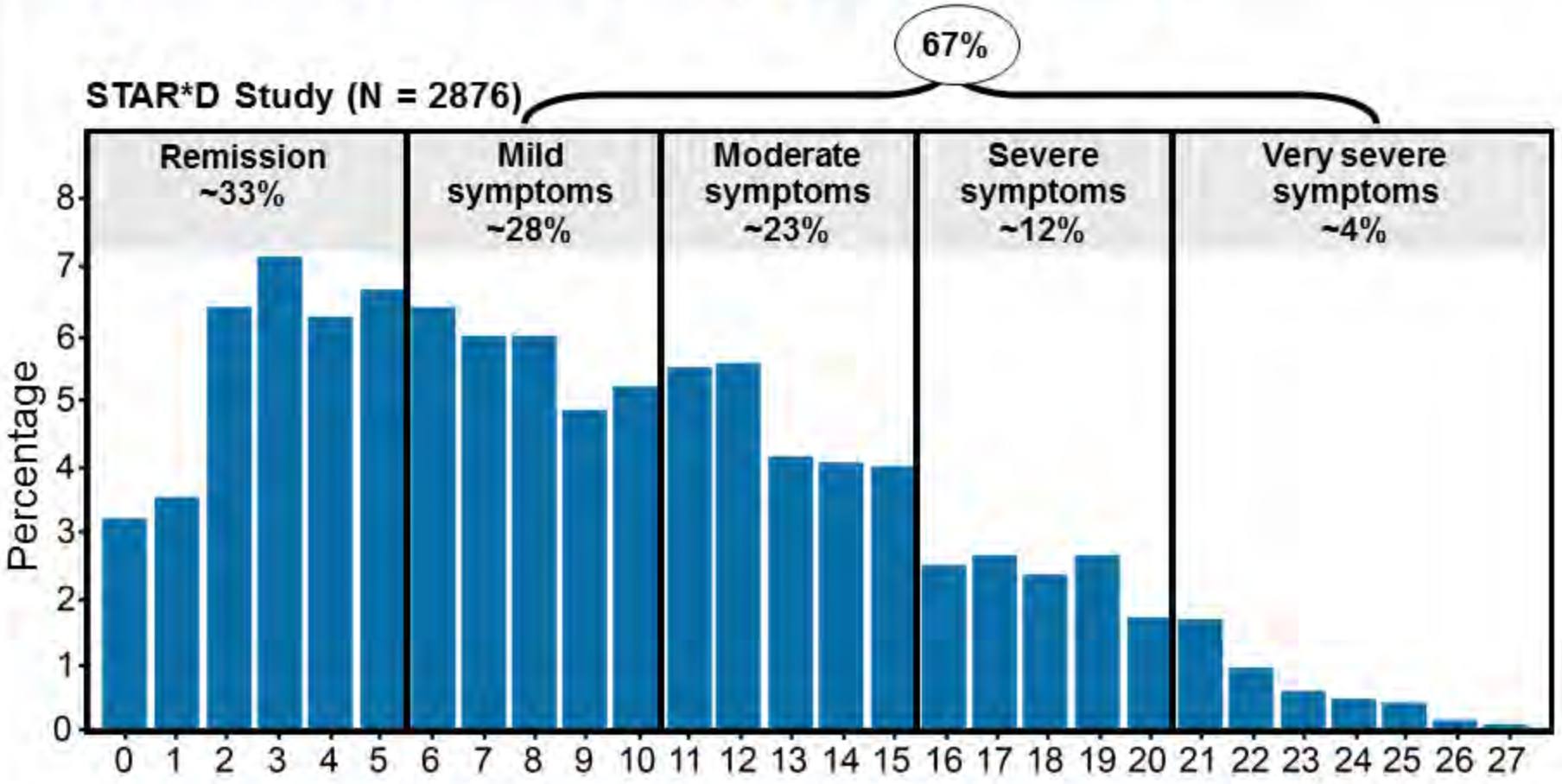
Augment T3

Level IV

Efexor + Mirtazapine

Trancyclopromine

Citalopram Response in STAR*D: Remission in Only One-Third

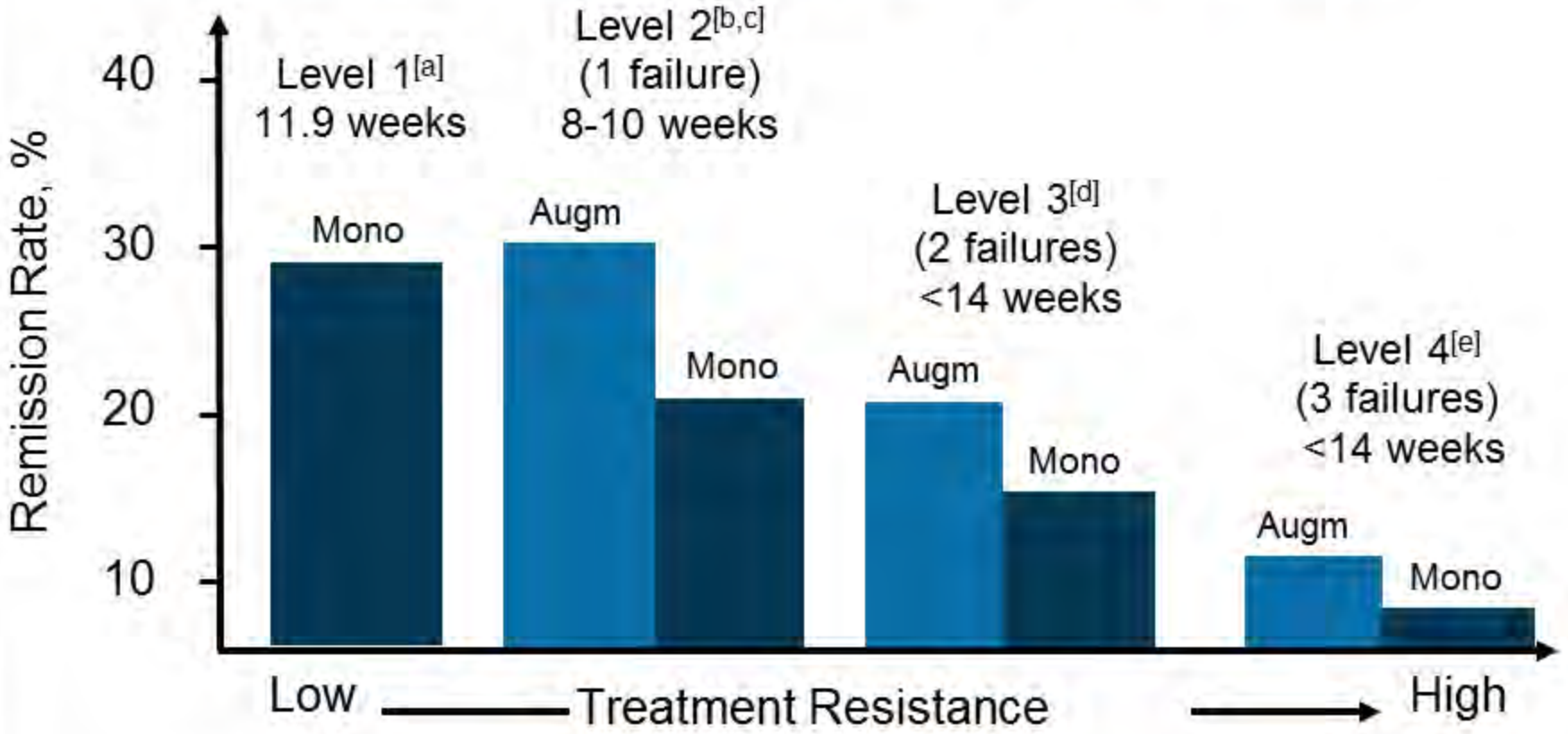


QIDS-SR = Quick Inventory of Depressive Symptomatology–Self-Report

Trivedi MH et al. *Am J Psychiatry*. 2006; 163:28-40.

Michael Thase 2011

STAR*D Clinical Study Results
Remission Rates (HAM-D-17 < 8)



Augm = augmentation treatment; HAM-D = Hamilton Rating Scale for Depression; Mono = monotherapy

a. Rush AJ, et al. *Am J Psychiatry*. 2006;163:1905-1917; b. Trivedi MH, et al. *J Clin Psychiatry*. 2006;67:1458-1465; c. Trivedi MH, et al. *N Engl J Med*. 2006;354:1243-1252; d. Nierenberg AA, et al. *Am J Psychiatry*. 2006;163:1519-1530; e. McGrath PJ, et al. *Am J Psychiatry*. 2006;163:1531-1541.


Where?

Where?

- Inpatient
- Residential
- PHP
- IOP
- Outpatient

- BUT most antidepressants are prescribed by PCP

Who Needs to Be Hospitalized for Depression?

- **People who are at risk of hurting themselves or others.**
- **People who are unable to function.**
- **People who need observation when trying a new medication (or a major medication overhaul).**
- **People who need treatments that are given only in a hospital (e.g. ECT).**

Many people start an antidepressant in the hospital, but if the medication effects are delayed by weeks, how do we account for the improvements that we see in only a few days?

a) Placebo effect

b) Therapeutic environment

c) Remove a specific life stressor

d) Therapeutic side effect (e.g. for sleep)


When?

When

- Research suggests that antidepressants can be helpful for people with moderate or severe depression.
- They're not usually recommended for mild depression, unless other treatments like exercise or therapy have not helped.
- A course of treatment usually lasts for at least 6 months after symptoms start to improve. Some people with recurrent depression may be advised to take them indefinitely.

- Start medication when symptoms of anxiety or OCD are impairing ability to function
- Start medication for depression when symptoms become moderate or behavioral interventions are impractical
- Compared to the pre-medication era (most of history), there seems to be relatively less severe, catatonic, and psychotic depression. Maybe because of the medications curbing the severity.

Predictive Value of Early Antidepressant Response

Metaanalysis[1] (Taylor, et al.)

- 28 randomized controlled trials (N = 5,872) of SSRIs vs placebo
- Treatment with SSRIs is associated with symptomatic improvement by the end of the first week of use
- Improvement continues at a decreasing rate for at least 6 weeks

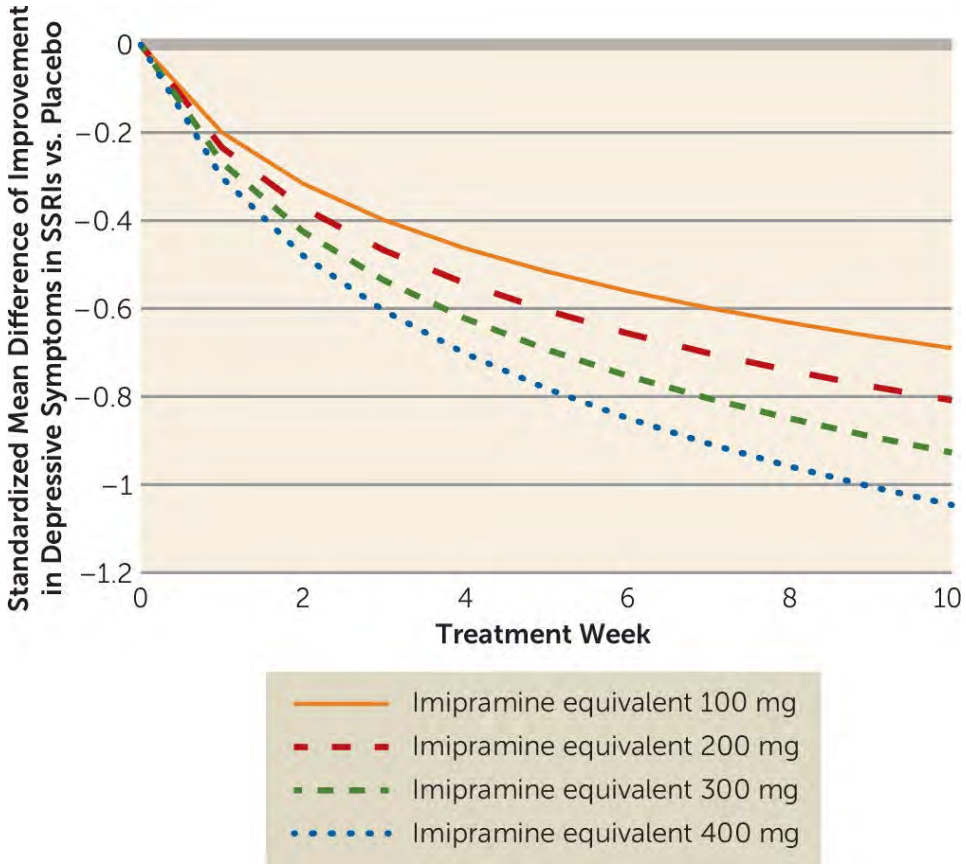
VAST-D Subanalysis[2]

- Odds of achieving response and remission at week 12 are greater among individuals who exhibit improvement by the end of week 2 of initial antidepressant treatment (OR 7.7 and 3.5, respectively)

1. Taylor. Arch Gen Psychiatry. 2006; 63:1217 2. Hicks. Psych Res Clin Pract. 2019;1:58.

Slide credit: clinicaloptions.com

Systematic Review and Meta-Analysis: Dose-Response Relationship of Selective Serotonin Reuptake Inhibitors in Major Depressive Disorder



Dose Equivalents:

100 mg imipramine

120 mg sertraline

100 mg fluoxamine

20 mg paroxetine

20 mg fluoxetine

33 mg Citalopram

16.7 mg escitalopram

Jakubovski et al Am J Psychiat Feb 2016

When treatment does not work, THINK

- Alcohol and other substance abuse
- Medical Illness
- Other prescribed or OTC medication
- Non-adherence with prescribed medication
- Personality or psychosocial factors

Augmentation Strategies: the art beyond the science

- Two (or more) antidepressants
  - Bupropion or mirtazapine + SSRI or SSNI
- Antipsychotic + antidepressant
  - Good data in psychotic depression
  - Fair data in refractory depression and OCD
- Lithium
- Other mood stabilizers
- Misc: buspirone (buspar), stimulants, atomoxetine (Strattera), folic acid, Thyroid Hormone


Why?

“chronic pain was the most common condition leading to an antidepressant prescription—even more so than for depression”

- Insomnia
- Parkinson's disease
- smoking cessation
- vasomotor symptoms of menopause

Remember we're prescribing "antidepressants" for a variety of psychiatric and nonpsychiatric indications

Table 1

Selective serotonin reuptake inhibitors

Medication	Psychiatric indication(s)	Nonpsychiatric indication(s)
Citalopram	*FDA-approved*: MDD[8] *Off-label*: BPSD,[9] BED,[10] GAD,[11,12] OCD,[13] PD,[14,15] PMDD,[16] PTSD,[17] SAD,[18] AUD[19]	*Off-label*: Premature ejaculation,[20] vasomotor symptoms of menopause[21]
Escitalopram	*FDA-approved*: MDD,[22] GAD[22] *Off-label*: BED,[23] BN,[24] OCD,[25,26] PD,[27] PMDD,[27,28] PTSD[29]	*Off-label*: Vasomotor symptoms of menopause[30,31]
Fluoxetine	*FDA-approved*: Bipolar I depression (when used with olanzapine),[6] BN,[6] MDD,[6] OCD,[6] PD,[6] PMDD[6] *Off-label*: BED,[32] PTSD,[33,34] SAD[35]	*Off-label*: Fibromyalgia,[7] premature ejaculation,[36] hot flashes (with history of breast cancer),[37] Raynaud's phenomenon[38]
Paroxetine	*FDA-approved*: GAD,[39] MDD,[39] OCD,[39] PD,[39] PMDD,[39] PTSD,[39] SAD[39] *Off-label*: None	*Off-label*: Premature ejaculation,[40] fibromyalgia,[41] headaches,[42] pruritus (nondermatologic)[43]
Sertraline	*FDA-approved*: MDD,[44] OCD,[44] PD,[44] PMDD,[44] PTSD,[44] SAD[44] *Off-label*: BED,[45,46] BN,[47] GAD[48]	*Off-label*: Premature ejaculation,[49,50] fibromyalgia[51]

AUD: alcohol use disorder; BED: binge eating disorder; BN: bulimia nervosa; BPSD: behavioral and psychological symptoms of dementia; GAD: generalized anxiety disorder; MDD: major depressive disorder; OCD: obsessive-compulsive disorder; PD: panic disorder; PMDD: premenstrual dysphoric disorder; PTSD: posttraumatic stress disorder; SAD: social anxiety disorder

Serotonin-norepinephrine reuptake inhibitors

Medication	Psychiatric indication(s)	Nonpsychiatric indication(s)
Desvenlafaxine	*FDA-approved*: MDD[52] *Off-label*: None	*Off-label*: Vasomotor symptoms of menopause[53]
Duloxetine	*FDA-approved*: GAD,[54] MDD[54] *Off-label*: None	*FDA-approved*: Fibromyalgia,[54] musculoskeletal pain (chronic),[54] diabetic neuropathy[54] *Off-label*: Stress urinary incontinence after prostatectomy[55,56]
Venlafaxine	*FDA-approved*: GAD,[57] MDD,[57] PD,[57] SAD[57] *Off-label*: OCD,[58,59] PTSD,[60] ADHD (pediatric patients only),[61,62] PMDD[63]	*Off-label*: Migraine prophylaxis (episodic),[64,65] diabetic neuropathy,[66] hot flashes (history of breast cancer),[67] peripheral neuropathy (due to chemotherapy)[68]

ADHD: attention-deficit/hyperactivity disorder; GAD: generalized anxiety disorder; MDD: major depressive disorder; OCD: obsessive-compulsive disorder; PD: panic disorder; PMDD: premenstrual dysphoric disorder; PTSD: posttraumatic stress disorder; SAD: social anxiety disorder

Table 4

Atypical antidepressants

Medication	Psychiatric indication(s)	Nonpsychiatric indication(s)
Bupropion	*FDA-approved*: MDD,[108] smoking cessation[108] *Off-label*: ADHD,[109] bipolar depression[110]	*Off-label*: SSRI-induced sexual dysfunction[111,112]
Mirtazapine	*FDA-approved*: MDD[113] *Off-label*: PD,[114,115] PTSD,[116] insomnia[117]	*Off-label*: Tension-type headache prophylaxis,[118] obstructive sleep apnea[119]
Trazodone	*FDA-approved*: MDD[120] *Off-label*: BPSD[121,122]	*Off-label*: Insomnia[123]

ADHD: attention-deficit/hyperactivity disorder; BPSD: behavioral and psychological symptoms of dementia; MDD: major depressive disorder; PD: panic disorder; PTSD: posttraumatic stress disorder; SSRI: selective serotoni

Medication	Psychiatric indication(s)	Nonpsychiatric indication(s)
Amitriptyline	*FDA-approved*: MDD[69] *Off-label*: None	*Off-label*: Fibromyalgia,[70] functional dyspepsia,[71] interstitial cystitis,[72,73] IBS,[74] migraine prophylaxis,[75,76] neuropathic pain (chronic),[77,78] postherpetic neuralgia,[79,80] sialorrhea (clozapine-induced)[81]
Amoxapine	*FDA-approved*: MDD[82] *Off-label:* None	*Off-label*: IBS[83]
Clomipramine	*FDA-approved*: OCD[84] *Off-label*: MDD,[85] PD[86]	*Off-label*: Ejaculatory disorders[87,88]
Desipramine	*FDA-approved*: MDD[89] *Off-label*: None	*Off-label*: Diabetic neuropathy,[90] IBS,[91] postherpetic neuralgia[92]
Doxepin	*FDA-approved*: MDD,[93] AUD,[93] GAD,[93] insomnia[93] *Off-label*: None	*Off-label*: Chronic idiopathic urticaria[94]
Imipramine	*FDA-approved*: MDD[95] *Off-label*: BN,[96] PD,[97] BED[98]	*FDA-approved*: Childhood enuresis (age ≥6)[95] *Off-label*: Neuropathic pain,[99] urinary incontinence,[100] diabetic neuropathy[92]

Why

- Antidepressants Get a Bad Rap. Why Do So Many Take Them?

What is the goal of treatment?

- Prescribing for depression or other symptoms is about helping to relieve a patient's acute suffering enough that they can return to normal functioning
- Goal of treating a major depressive episode is total remission of symptoms AND working to prevent recurrence

Why

- Going back to the question about antidepressants preventing suicide: is this true?
- Mass prescribing doesn't seem to correlate with lower suicide rate
- The only medications with a clear "anti-suicide" effect are Lithium and Clozapine (an antipsychotic)
- suicide might be prevented by the treatment of depression, but it is a much stronger claim that 'treatment with antidepressants prevents suicide'

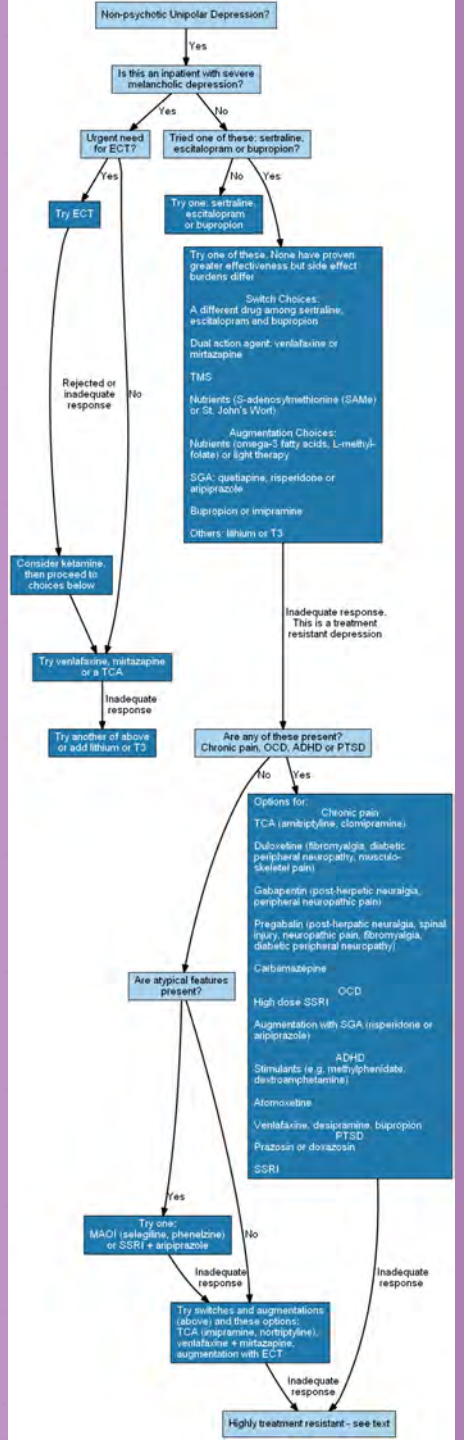
- social factors like poverty, homelessness, isolation, and lack of education play a significant role in all illnesses and require at least as much attention as a patient's physiological problems. Indeed, social determinants of health (SDOH) contribute about three-quarters of the risk for all human illness.
- Pills won't fix a broken life or a dysfunctional society
- Pills won't change who someone fundamentally is (i.e. cosmetic psychopharmacology)

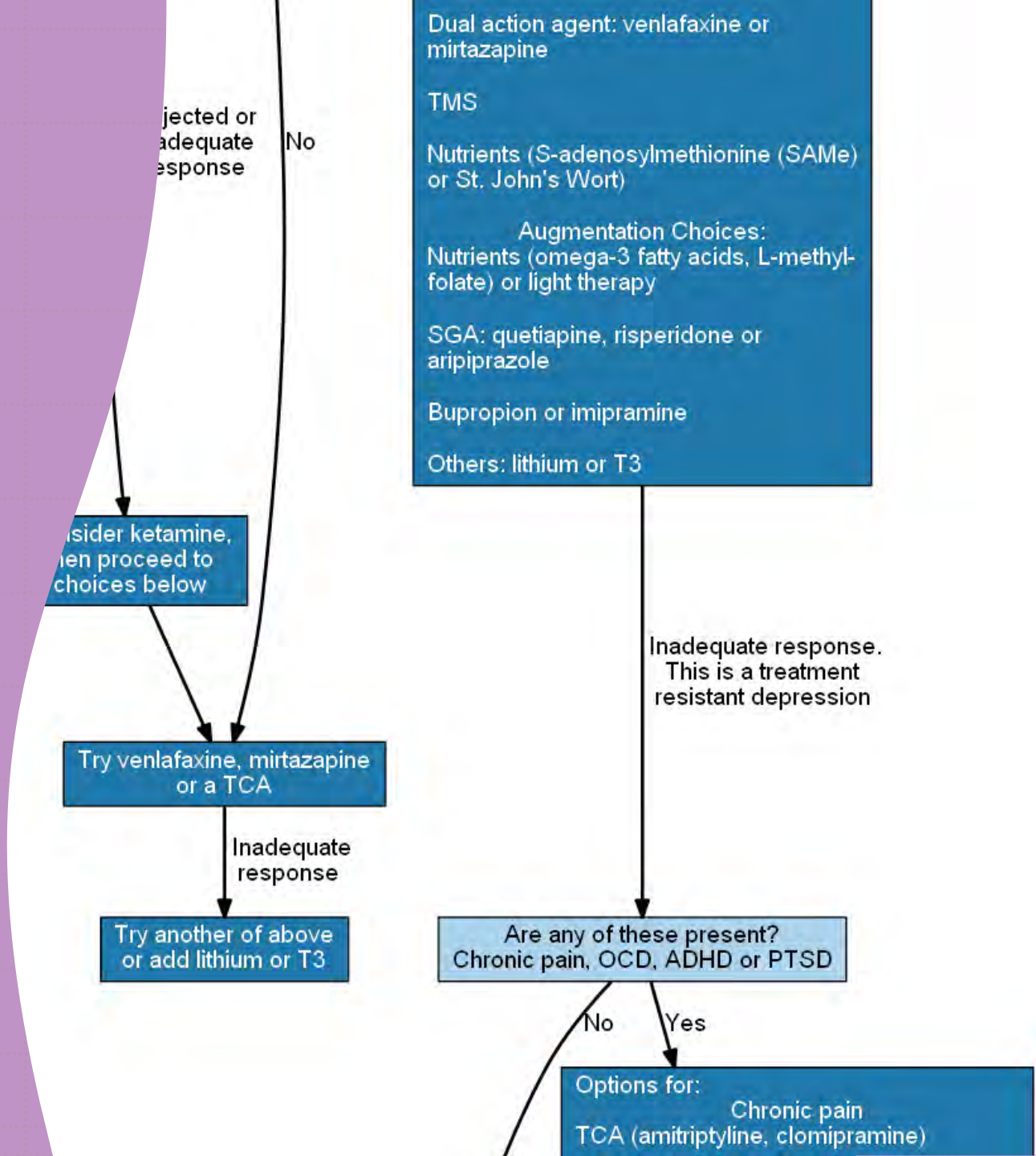
How? (The domain of prescribers)

- Example of an algorithm for treating non-psychotic depression

https://psychopharm.mobi/algo_live/#

Authors
Chistoforos I. Giakoumatos
David N. Osser, M.D.




jected or
adequate
esponse
No
Dual action agent: venlafaxine or mirtazapine
TMS
Nutrients (S-adenosylmethionine (SAMe) or St. John's Wort)
Augmentation Choices:
Nutrients (omega-3 fatty acids, L-methyl-folate) or light therapy
SGA: quetiapine, risperidone or aripiprazole
Bupropion or imipramine
Others: lithium or T3
sider ketamine,
en proceed to
choices below
Try venlafaxine, mirtazapine or a TCA
Inadequate response
Try another of above or add lithium or T3
Inadequate response. This is a treatment resistant depression
Are any of these present?
Chronic pain, OCD, ADHD or PTSD
No
Yes
Options for:
Chronic pain
TCA (amitriptyline, clomipramine)

Thank you for your attention!

Aaron Owen, MD
aowen3@wisc.edu

UW Health Department of Psychiatry

Join on February 22: Ketamine with Dr. Steven Garlow, MD, Ph.D