Late Life Depression and Anxiety

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FACULTY/PRESENTER DISCLOSURE

- Faculty: C. Omelan
- No conflict of interest to declare
- Relationships with commercial interests:
  - Grants/Research Support: None
  - Speakers Bureau/Honoraria: None
  - Consulting Fees: None
  - Other: Employee of WRHA, SBGH, HSC

DECLARATION OF CONFLICTS OF INTEREST

- I will discuss off-label use of medications (quetiapine)

OBJECTIVES

- Review new research about metabolism and brain health
- Explain the limitations of pharmacotherapy
- Discuss evidence-based options for treatment

CAVEAT

- My comments apply primarily to ***late onset (>60)*** depression and anxiety
  - i.e. *first onset* of depressive symptoms in older age
- *Not those with a long history of a mood disorder*
  - For these patients, the management is similar to younger people

CASE: VC

- 82 yo widowed female c/o depressed mood & worry re: her health
- Physical exam, lytes, TSH , B12, CT scan are normal
- PHQ 9 = 10 (≥ 10 suggests depression)
- Current Rx:
  - zopiclone 7.5 mg po at HS
  - lorazepam 1 mg in am
  - citalopram 40 mg
- What do you do?

DEPRESSION

AUDIENCE Q'S

- What is the typical improvement over placebo seen with antidepressants?
- What *serious* adverse events may be seen with SSRI's?
- What nonpharmacological interventions have evidence for efficacy in depression?

AUDIENCE Q'S

- Which drugs have RCT evidence in late life depression?
- Which drug may work *faster* in depression?

EPIDEMIOLOGY

- Depression is the most common *mental health* problem for older adults

Canadian Coalition for Seniors' Mental Health National Guidelines 2006.

MDD occurs in ~ 5% of community-dwelling older adults

NEJM 371;13 nejm.org September 25, 2014

LATE LIFE DEPRESSION

- *Late-life depression* is defined as MDD in people ≥ 60-65 years of age
- First presentation of depression in late life is **not typical**

NEJM 371;13 nejm.org September 25, 2014

LATE LIFE DEPRESSION

- Compared to patients with earlier onset of depression, LLD:
  - has a worse prognosis,
  - a more chronic course,
  - a higher relapse rate, and
  - higher levels of medical comorbidity, & cognitive impairment,
  - increased mortality.

CANMAT Guidelines Can J Psych 2016, Vol. 61(9) 588-603

LLD: EPIDEMIOLOGY

- Depressive *symptoms* affect 15% of community living elderly

CCSMH, 2006

- Rates increase with other morbidity:
  - 5 - 10% in primary care
  - 37% in critical care hospitalizations

CIHI 2010

.

LATE LIFE DEPRESSION

- LLD doubles the risk of *dementia*[1]
- Depression is both a risk factor *for* and a prodrome *of* dementia[2]
- Prevalence of mild cognitive impairment (MCI) in LLD is ~ 54%[3]
- *(In some cases it **is** early dementia)*

[1] Cherbuin N. BMJ Open 2015;5 doi:10.1136
[2] Farioli-Vecchioli Current Neuropharmacology, 2018, 16, 308-326
[3] Ismail Z. Neurodegener Dis Manag. 2014;4:119-126.

LATE LIFE DEPRESSION

- This cohort may be more comfortable with seeing a doctor for *physical* reasons.
  - can present with bodily symptoms (pain, bowel complaints)

Table 1. Presentation of depression in the elderly: X *indicates the symptom is prominent;* XX *indicates the symptom is very prominent.*

TYPICAL SYMPTOMS	PROMINENT IN ELDERLY PATIENTS	PROMINENT IN YOUNGER PATIENTS
SIG E CAPS		
• Sleep (insomnia or excess sleep)	XX	X
• Interest (anhedonia)	X	X
• Guilt	X (often feeling a burden to family)	XX
• Energy	XX	X
• Concentration	X	X
• Affect (dysphoria)		XX
• Psychomotor changes	XX	X
• Suicide	X (higher rate, especially for older men)	X
Other		
• Anxiety	XX	X
• Decreased appetite or weight loss	X	X
• Complaints of memory loss	XX	
• Pain	X	
• Fatigue	XX	X

Data from the Canadian Coalition for Seniors' Mental Health.[1]

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(Use "✔" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3

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THEORIES OF LATE LIFE DEPRESSION

- Executive Dysfunction Syndrome hypothesis
- The Vascular Depression hypothesis
- The Inflammation hypothesis
- Gut Microbiota hypothesis
- The Neurogenesis hypothesis

Alexopoulos Translational Psychiatry (2019)9:188

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Alexopoulos Translational Psychiatry (2019)9:188

THE NEUROGENESIS HYPOTHESIS

- Evidence for neurogenesis in depression & anxiety is strong (but *not conclusive)*
- Late onset depressive symptoms often ***predate dementia***
- Anxiety and depression may anticipate memory problems by years

THE VIRTUOUS CIRCLE

- A ***virtuous circle***[1] appears to maintain brain health

[1]Nehls M. Journal of Molecular Psychiatry (2016) 4:3

THE VIRTUOUS CIRCLE = HUNTER GATHERING

- "What did our ancestors do?"
  - ***Switched metabolic gears*** (got hungry)
  - ***Bright light*** (waited for daytime)
  - ***Socialized*** (formed a group)
  - ***Exercised*** (ran down prey)
  - ***Navigated*** (mapped where food was)
  - ***Novel stimuli*** (saw unfamiliar things)
  - Adequate ***sleep*** (rested)

Nehls M. Journal of Molecular Psychiatry (2016) 4:3

THE VIRTUOUS CIRCLE

- Successful adaptation tied *brain health* to *foraging*
- Activities related to hunting made us ***lean*** & ***muscular;***
  - This offers the greatest chance of *finding food* and *getting home*
- There is a **calorie-centric** evolutionary reason for brain neuroplasticity

Nehls M. Journal of Molecular Psychiatry (2016) 4:3

KEY CONCEPTS

- Healthy brains appear to rejeunvenate and regenerate
- ***depression*** & ***anxiety*** **may** be the subjective *experience of* inadequate cellular renewal

Mattson MP. Trends in Cognitive Sciences, March 2019, Vol. 23, No. 3

KEY CONCEPTS

- Antidepressants by themselves ***are only modestly effective***, as they do not address other aspects of the circle
- Maintaining a normal mood, & low anxiety levels involves factors tied to our needs

Mattson MP. Trends in Cognitive Sciences, March 2019, Vol. 23, No. 3

CUES FOR CELLULAR RENEWAL

- The basic requirements for brain health were provided for by a pre-modern way of life.
- But, being sedentary, lonely, having chronic stress, with a constant (ad libitum) eating pattern,
- Is a ***negative regulator*** *of subcellular renewal*, with detrimental consequences (anxiety & depression)

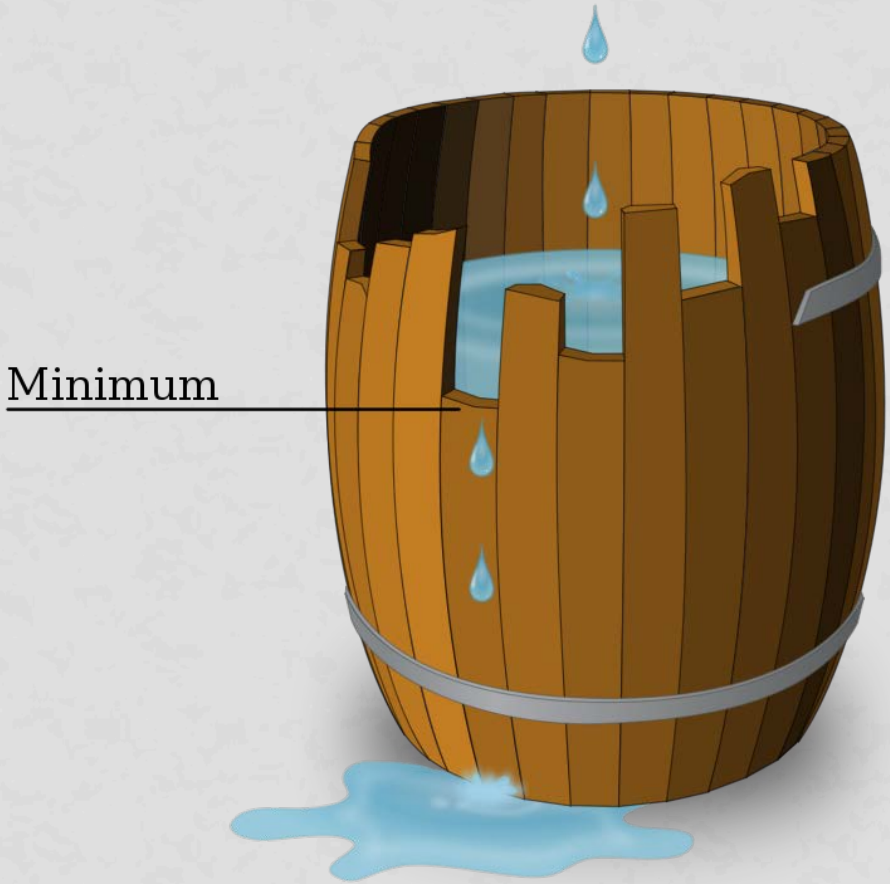
Nehls M. Journal of Molecular Psychiatry (2016) 4:3

THE LAW OF THE MINIMUM

- The Law of the Minimum dictates that the ***scarcest factor*** limits growth

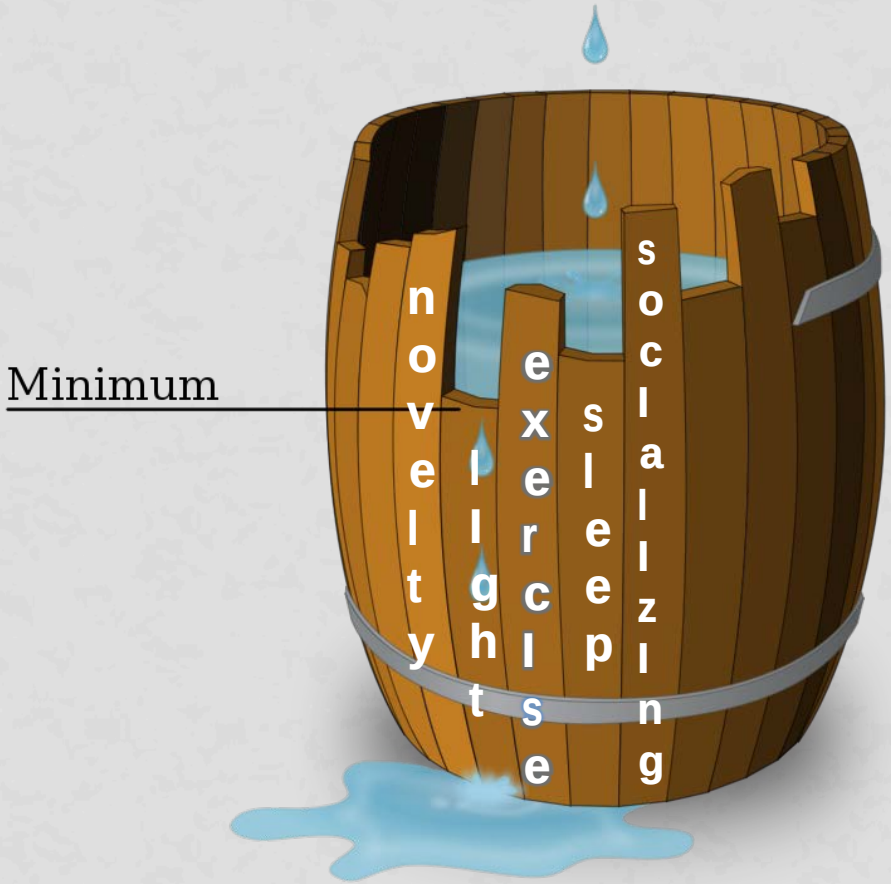
Nehls M. Journal of Molecular Psychiatry (2016) 4:3

Liebig's Law of The Minimum



By DooFi - Own work, Public Domain, https://commons.wikimedia.org/w/index.php?curid=6627159

Liebig's Law of The Minimum



A HYPOTHESIS

- Depression and anxiety symptoms signal a break in the ***virtuous circle***
- It doesn't matter how much of one factor you get
- The persistent ***lack of one element*** *(e.g. social contact)* may cause depressive symptoms to begin

HIPPOCAMPAL NEUROGENESIS

- ~700 neurons are added in the hippocampus each day
- there is an annual turnover of ~1.8 % of the neurons,
- a modest decline is seen during aging.

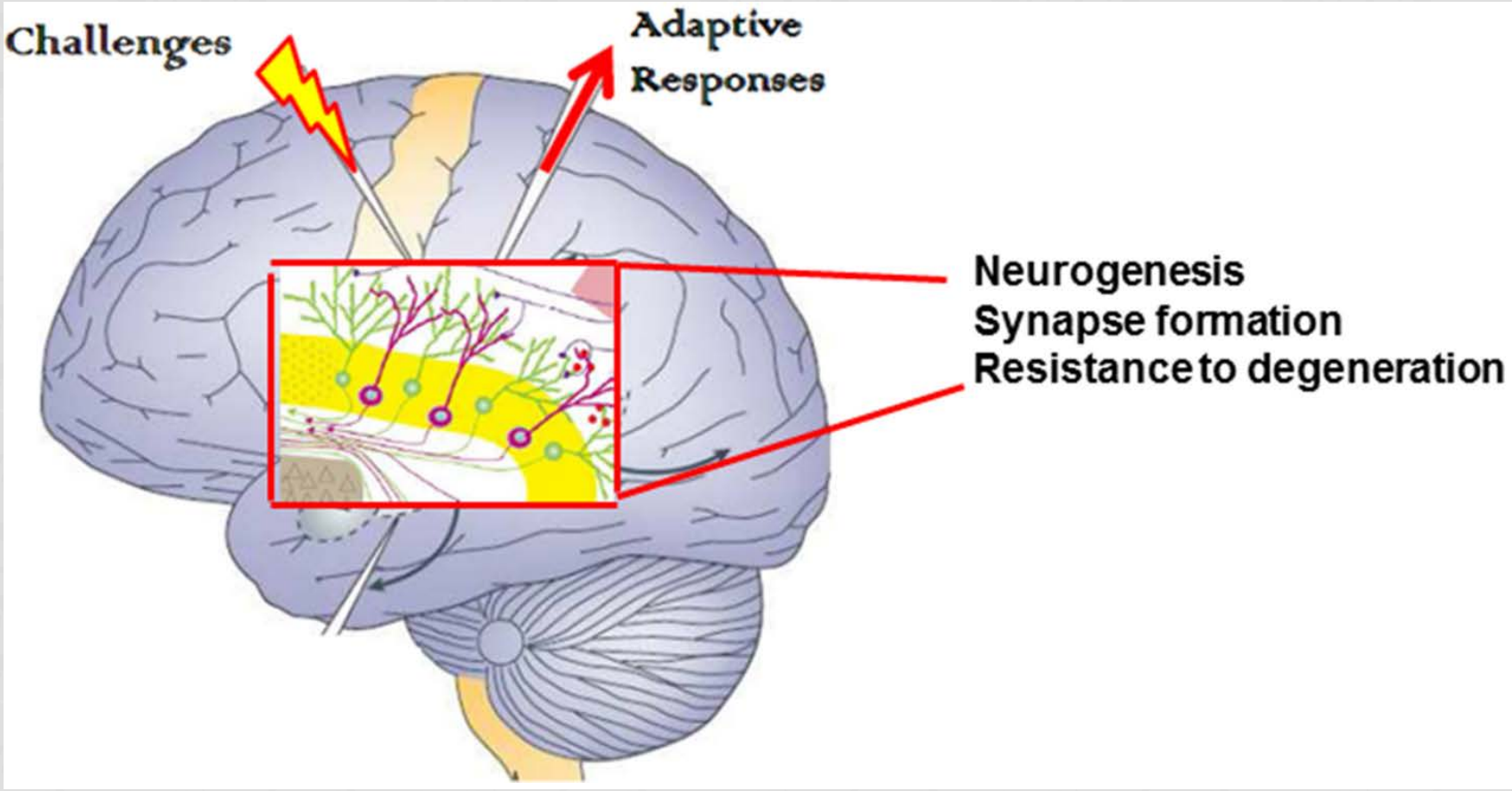
Horgusluoglu E. Am J Med Genet B Neuropsychiatr Genet. 2017 January ; 174(1): 93–112.

NEUROGENESIS

- New hippocampal neurons appear to be necessary for:
  - spatial navigation (useful in hunting),
  - episodic learning and memory retrieval
  - **regulation of mood**
  - **psychological resilience (resistance to stress)**
  - **reduction in anxiety**

Nehls M. Journal of Molecular Psychiatry (2016) 4:3

EUSTRESS



Mattson MP. *Dose-Response*, 12:600–618, 2014

ADULT HIPPOCAMPAL NEUROGENESIS

- Senescent mice maintained in enriched environments show ***a fivefold*** increase in AHN[1].
- Forced social isolation ***inhibits*** AHN.[2]

1. Kempermann G. Ann Neurol. 2002;52(2):135–43.

2. Nehls M. Journal of Molecular Psychiatry (2016) 4:3

AHN IN DEPRESSION

- SSRI's lose their antidepressant effects when neurogenesis is prevented.

Peng L. Am J Pathol 2018, 188:

SSRI's May Slow Dementia

- Escitalopram lowers β Amyloid.[1]
- In patients with a previous hx of depression,
- SSRI's may slow the conversion of mild cognitive impairment (MCI) to dementia[2]

[1]Sheline YV. Neurology 2020
[2]Bartels, C. Am. J. Psychiatry 175, 232–241 (2018).

EXERCISE & HIPPOCAMPAL VOLUME

- After 1 year , an aerobic exercise group showed an **increase** in hippocampal volume of ~ 2 %,

- A stretching (yoga) control group demonstrated a 1.4 % **decline in volume** over the one-year interval,

Nehls M. Journal of Molecular Psychiatry (2016) 4:3

Exercise

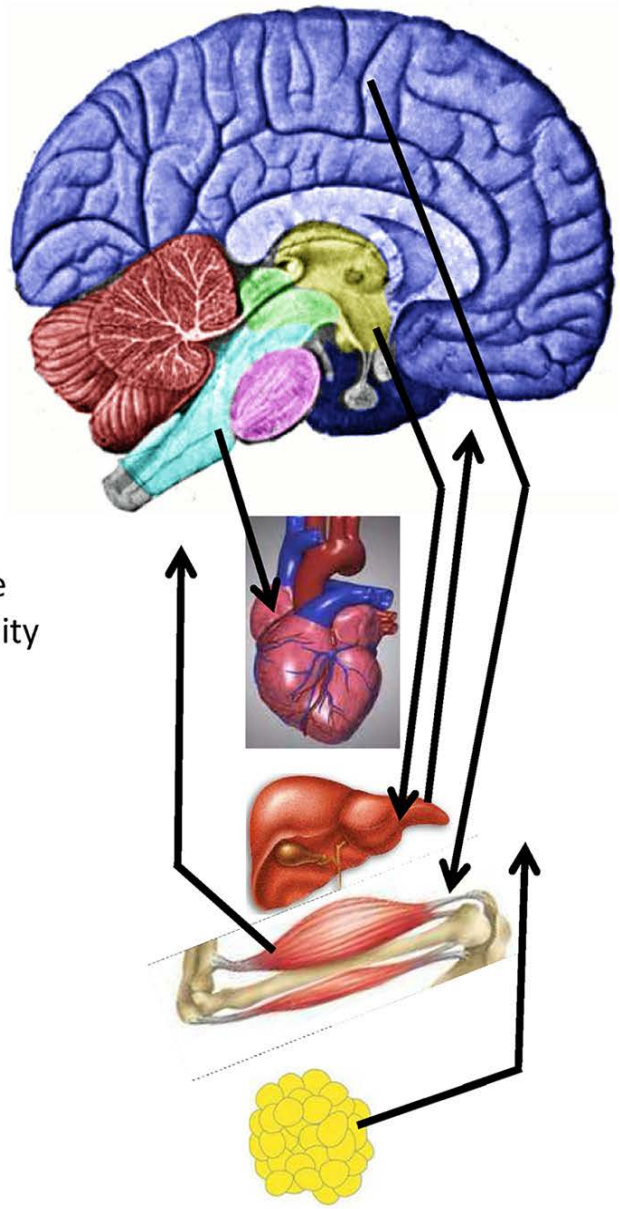
Neurogenesis
Synaptogenesis
Synaptic plasticity
Cognitive function
Motor function
DNA repair
Mitochondrial biogenesis
Reduced inflammation

Decreased resting heart rate
Increased heart rate variability
Decreased blood pressure

Increased insulin sensitivity
Ketone body production

Increased insulin sensitivity

Fatty acid mobilization
Reduced inflammation



Intermittent Fasting

Neurogenesis
Synaptogenesis
Synaptic plasticity
Cognitive function
Motor function
Reduced inflammation
Enhanced autophagy

Decreased resting heart rate
Increased heart rate variability
Decreased blood pressure

Increased insulin sensitivity
Ketone body production

Increased insulin sensitivity

Fatty acid mobilization
Reduced inflammation

van Praag J Neurosci 2014; 34(46) 15139-15149

PHARMACOTHERAPY OF LLD

Ideal drugs	Real drugs
Large benefits	Modest benefits
Harmless	Some potential for harm
Well tolerated	Generally well-tolerated
Linear pharmacokinetics	Some are non-linear
Predictable half-life	Variable: short - long t / 2
Few drug-drug interactions (DDI)	Frequent DDI

TX OF LLD

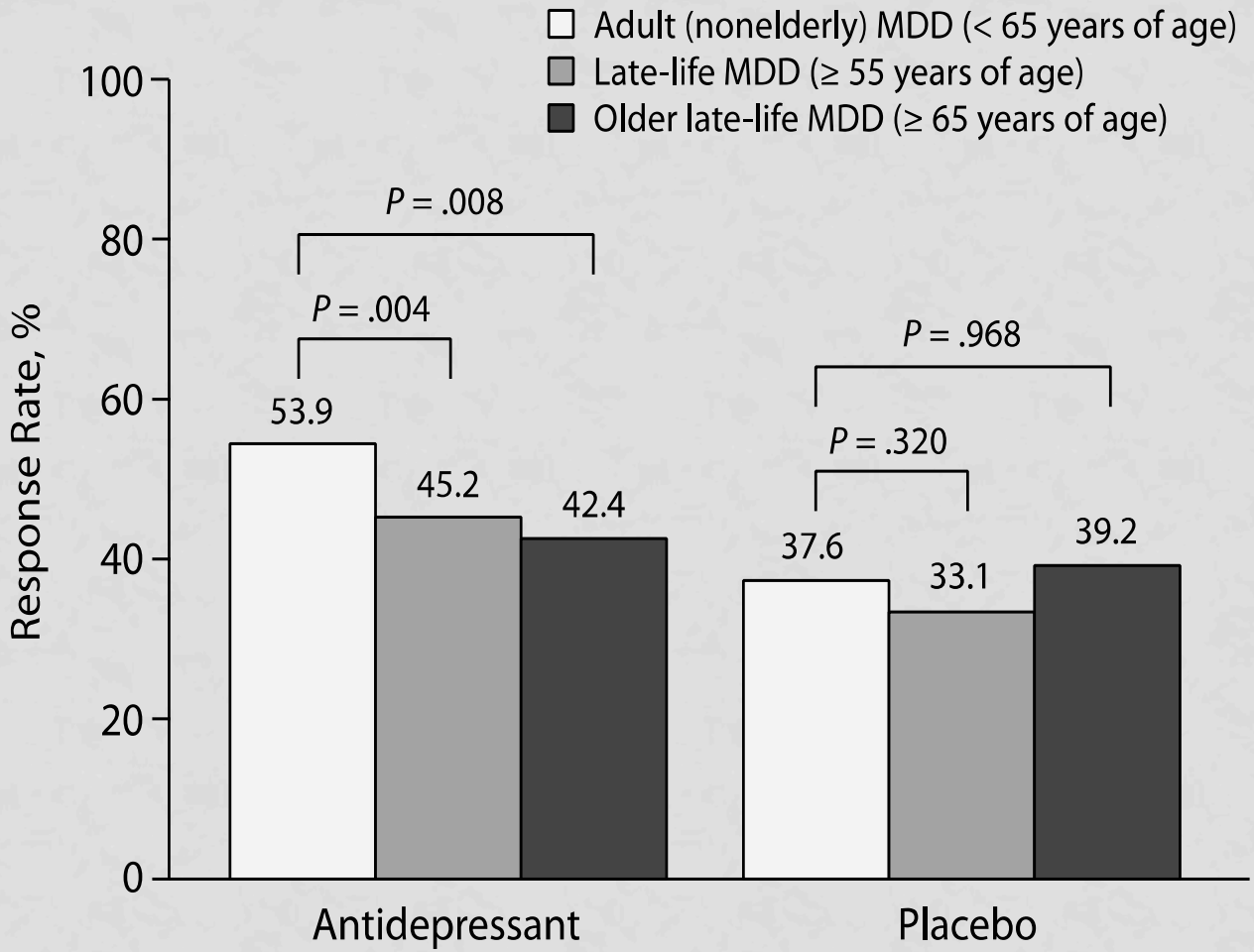
- ~14% of older adults are on an antidepressant

Mojtabai R. J Clin Psychiatry 2014;75(2):169–77.

But Do SSRI's *Work*?

- Meta-analyses suggest that antidepressants are ***only marginally more effective than placebo.***
- ***average HDRS change is ≈ 1.9-2.7 pts*** depending on the study
- ***NICE criteria for min. clin. sig. Δ is 3 points***
- ?an example of the Law of the Minimum?

Figure 3. Comparison (using analysis of variance) of Antidepressant and Placebo Response Rates in Younger Adult and Older Adult Patients[a]



Tedeschini E.J Clin Psychiatry 2011;72(12):1660–1668

NUMBER NEEDED TO TREAT

- The NNT for antidepressants in patients with LLD is:
- **6.7** (95% CI 4.8–10) *to achieve 1 more* ***response*** *than placebo (PBO)*.
- **14.4** *to achieve 1 more* ***remission*** than PBO (95% CI 8.3–50)

Kok, RM. J. Affect. Disord. 141, 103–115 (2012).

Table 6. Algorithmic Pharmacological Treatment of Late-Life Depression.

Recommendation	Treatment	Level of Evidence
First line	Duloxetine, mirtazapine, nortriptyline	Level 1
	Bupropion, citalopram/escitalopram, desvenlafaxine, duloxetine, sertraline, venlafaxine, vortioxetine	Level 2
Second line	Switch to	
	Nortriptyline	Level 1
	Moclobemide, phenelzine, quetiapine, trazodone	Level 2
	Bupropion	Level 3
	Combine with	
	Aripiprazole, lithium	Level 1
	Methylphenidate	Level 2
Third line	Switch to	
	Amitriptyline, imipramine	Level 2
	Combine SSRI or SNRI with	
	Bupropion, SSRI	Level 3

SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

CANMAT Guidelines Can J Psych 2016, Vol. 61(9) 588-603

TIME TO RESPONSE LONGER IN LLD

- Meta-analyses suggest that longer antidepressant treatment trials (10-12 weeks) are required in LLD.

Nelson JC, Am J Geriatr Psychiatry. 2008;16: 558-567.

DRUGS WITH EVIDENCE IN LLD

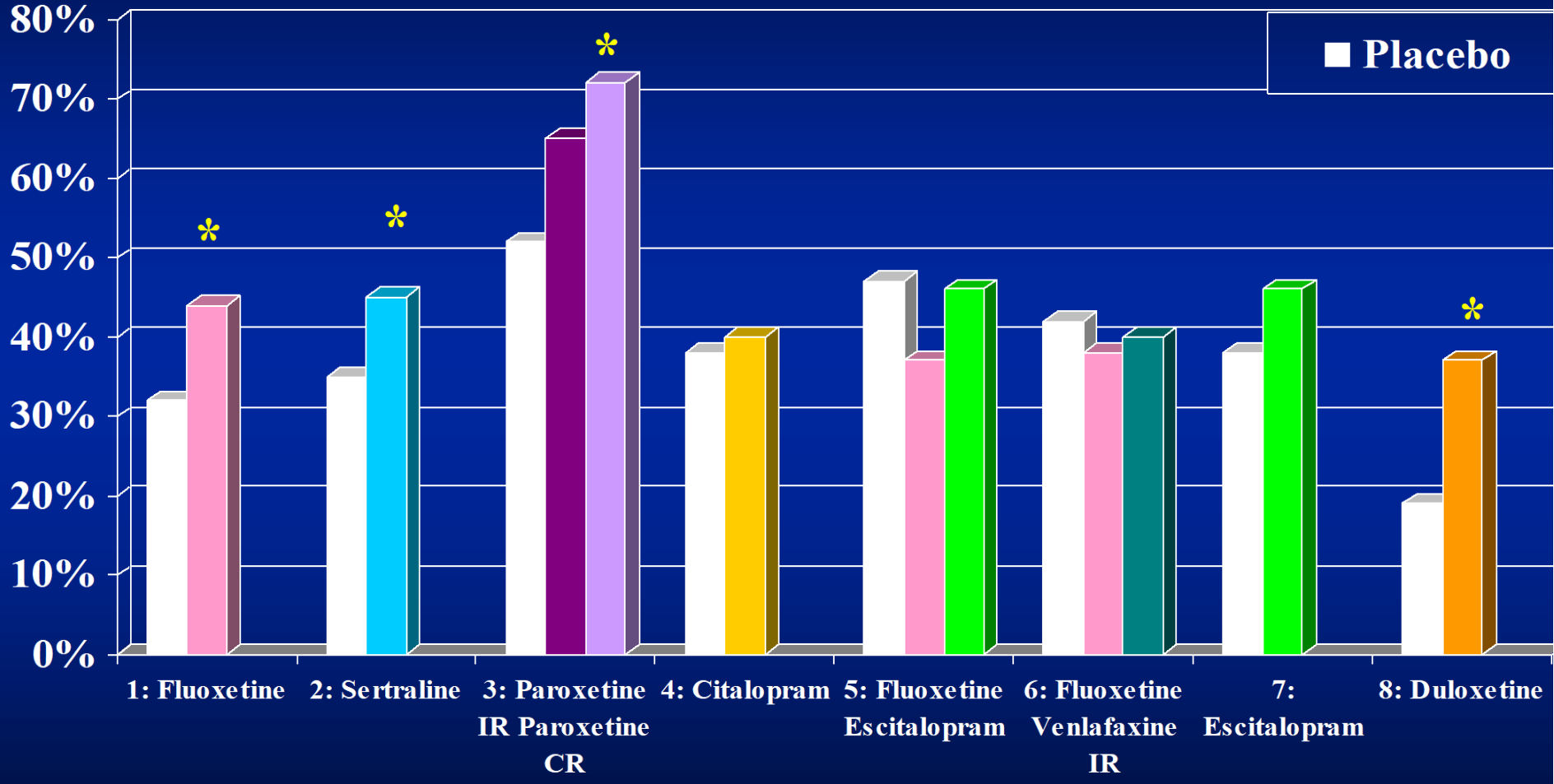
- **Sertraline (✔)**
- **Duloxetine (✔)**
- **Fluoxetine (x)**
- **Paroxetine (x)**
- **Quetiapine monotherapy (x)**

*I would **not** recommend for first line use*

- *Agomelatine (n/a) Vortioxetine (Trintellix)*[1]
- Citalopram (> 75 with HDRS >24)[2]
- *No evidence for escitalopram, venlafaxine, or mirtazapine*

[1]Katano C. International Clinical Psychopharmacology 2012, Vol 27 No 4
[2] Roose SP, et al. Am J Psychiatry 2004;161:2050-2059.

Response Rates (%) in Eight Published Randomized Placebo-Controlled Trials



1. Tollefson et al (1995) Int Psychogeriatrics; 7:89–104 – 2. Schneider et al (2003) Am J Psych; 160:1277-85 – 3. Rapaport et al (2003) J Clin Psych; 64:1065–74 – 4. Roose et al (2004) Am J Psych; 161:2050-9 – 5. Kasper et al (2005) Am J Geri Psych; 13:884-91 – 6. Schatzberg & Roose (2006) Am J Geri Psych; 14:361-70 – 7. Bose et al. (2008) Am J Geri Psych; 16:14-20 – 8. Raskin et al (2007) Am J Psychiatry; 164:900-9

Source: Benoit H. Mulsant, MD

TREATMENT RESISTANT LLD

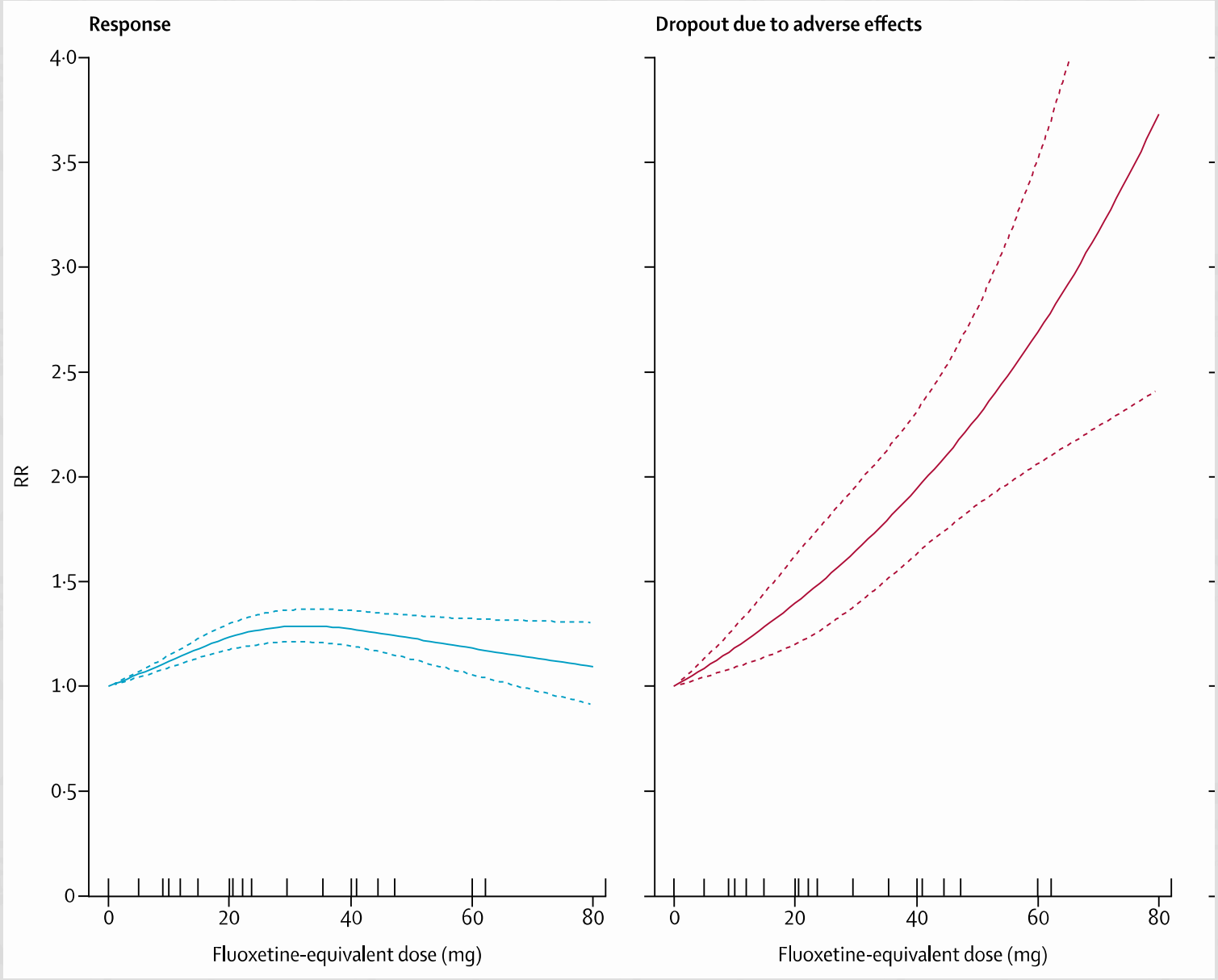
- Adding aripiprazole (Abilify) (10 -15 mg) to venlafaxine (Effexor) (150-300 mg) improved response in treatment resistant LLD
- NNT with aripiprazole was **6.6** [95% CI 3.5–81.8].
- Aripiprazole pts had more
  - akithisia **26%** (vs 12%) &
  - parkinsonism **17%** (vs 2%)

Lenze EJ. Lancet 2015; 386: 2404–12

MIRTAZAPINE IS FASTER?

- Evidence from 7 trials comparing mirtazapine to fluoxetine, citalopram, paroxetine and sertraline showed:
- ***Mirtazapine has a faster onset of action***

SSRI Dose Response and AE Curves



Furakawa T. Lancet Psychiatry 2019; 6: 601–09

MAINTENANCE TX

- Rates of relapse after discontinuation of treatment may be higher in older patients

Rost K. *BMJ* 2002;325(7370):934.

- Treatment should be continued for **12 months** *from the time of remission* (and up to 2 years)

CCSMH, 2006

ADVERSE EFFECTS OF RX

CONCERNS WITH A/D IN ELDERLY

- Efficacy
- Falls & orthostatic hypotension[1]
- Risk of bleeding [2]
- Anticholinergic effects
- SIADH picture (dilutional hyponatremia)
- Bone fragility
- Suicidality[3]
- Changes in sleep architecture
- Stroke
- QT prolongation/ cardiotoxicity
- Increased mortality

[1]Sterke CS. Br J Clin Pharmacol 2012;73:812-820
[2] Andrade C. J Clin Psch 2010;71(12) 1565-1575
[3]Juurlink et al (2006) Am J Psych; 163:813-21

Risk of Bleeding with SSRI's

Table 4 | Risk of upper gastrointestinal bleeding as a function of current use of SSRIs, aspirin, and other NSAIDs.

Medications used	Adjusted odds ratio (95% CI)
SSRI alone	1.7 (1.01–2.8)
Aspirin alone	2.4 (1.72–3.3)
Other NSAIDs alone	4.3 (3.7–5.1)
SSRI and aspirin, no other NSAIDs	3.0 (0.96–9.2)
Aspirin and other NSAIDs, no SSRI	13 (8.7–20)
SSRI and other NSAIDs, no aspirin	8.0 (4.8–13)
SSRI, aspirin, and other NSAIDs	28 (7.6–103)

Adapted from Dall et al. (2009).

Andrews PA. Frontiers in Psychology 2012;3(117):1-19

ANTICHOLINERGIC SIDE EFFECTS

- Avoid 3° amine TCA's
  - amitriptyline, imipramine
  - also cause orthostatic hypotension
- 2° amines preferable
  - nortriptyline, desipramine
- 30 mg paroxetine is more anticholinergic than 50 mg nortriptyline

Chew ML. Am Geriatr Soc 56:1333–1341, 2008.

HYPONATREMIA

- SIADH picture (dilutional hyponatremia)
  - > frequent in elderly
  - ranges from 12 to 39 % of those starting an SSRI[2]
  - usually 7-14 days into tx[1]
  - sometimes after increased fluid ingestion
  - Check Na^+ 2 weeks after initiation

[1] Frank C. Can Fam Physician 2014;60:121-6
[2] Arch Intern Med. 2004;164:327-332

FALLS

- Fall risk increases with antidepressant use.
  - dose-related for TCA's , not for SSRI's
  - **RR 1.9** for SSRI's

Thapa NEJM 1998

CITALOPRAM HPB WARNING

- A thorough QT study, conducted according to international standards, assessing the effects of citalopram 20 mg per day and 60 mg per day on the QT interval has shown that citalopram causes dose-dependent QT prolongation.

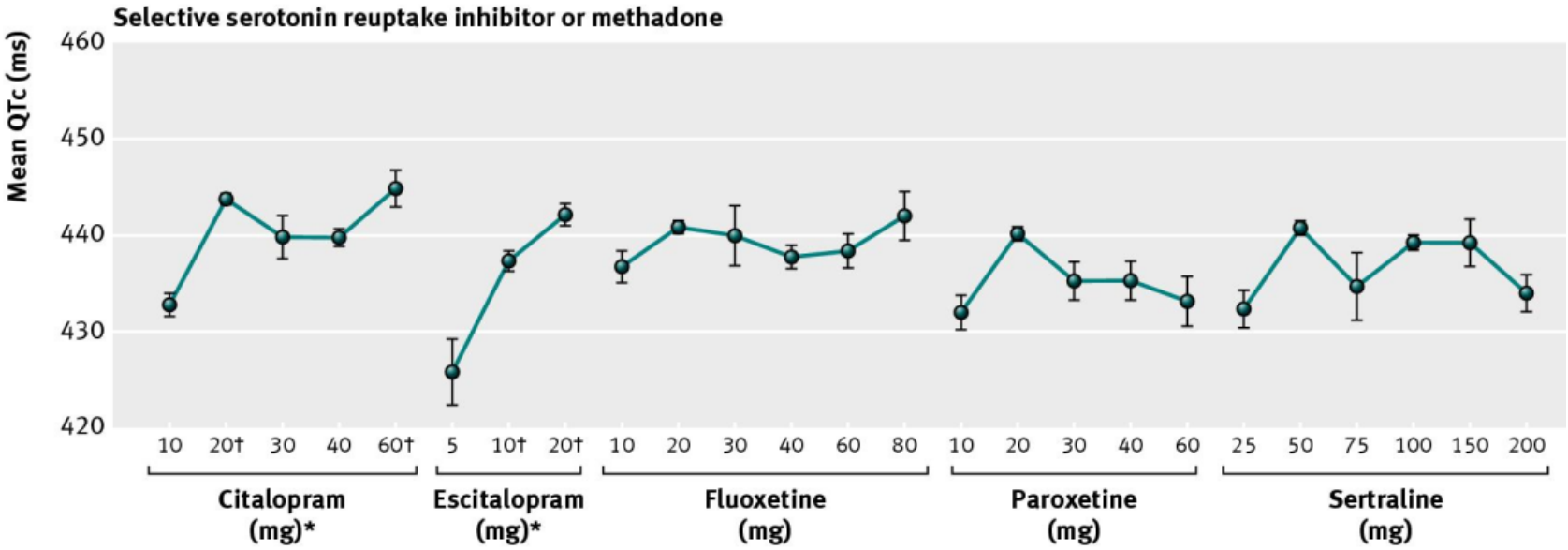
- Celexa® (citalopram hydrobromide) should no longer be prescribed at doses greater than 40 mg per day.

- 20 mg per day is the maximum recommended dose for patients with hepatic impairment, patients who are 65 years of age or older, patients who are CYP2C19 poor metabolizers, or patients who are taking concomitant cimetidine or another CYP2C19 inhibitor.

- Celexa® (citalopram hydrobromide) is contraindicated in patients with congenital long QT syndrome or known QT interval prolongation.

SSRI'S & QT INTERVAL

Figure



Castro VM. BMJ 2013;346:f288 doi: 10.1136/bmj.f288

OTHER DRUGS TO AVOID

- **Fluoxetine** (long metabolite half life, activating, unfavorable pharmacokinetics with age)
- **Paroxetine** (anticholinergic effects, non-linear pharmacokinetics)

NON PHARM TREATMENT OF LLD

NON PHARM TX OF LLD

- Psychotherapy has evidence in LLD:
  - ***Cognitive behavioral therapy(CBT)***
  - Problem solving therapy (PST)[1]
  - Brief dynamic therapy
  - Interpersonal therapy (IPT)
  - Reminiscence therapy

[1] PST has been proven efficacious in depression with executive dysfunction Kiosses DN. JAMA Psychiatry. 2015 January ; 72(1): 22–30

NON PHARM TX OF LLD

- There is evidence that:
  - improved socializing
  - life review
  - music therapy, &
  - exercise

  can *prevent* and *improve* depression
  (Grade A recommendation)

CCSMH National guidelines for seniors' mental health. 2006.

LIGHT THERAPY

- RCT evidence in LLD[1]
- **Light therapy** can be added to medication for *nonseasonal* mild to mod. MDD[2].
- Most effective when given during the first week of antidepressant treatment.
  - 10,000 lux /30 mins/ day in early am.
  - 12–18 inches from the unit with their eyes open.

[1]Lieverserch R. A Gen Psychiatry. 2011;68(1):61-70
[2]McMaster PBSG EDUCATIONAL MODULE Vol. 22 (2), February 2014

LIGHT THERAPY

- One RCT in adults found a standard course of **light therapy** *as effective as fluoxetine* 20 mg
  - 67% response rates (for each)
  - 50% & 54% remission rates (respectively).
- Light treatment showed an **earlier response** onset and **lower rate of side effects** compared with fluoxetine.

EXERCISE

- RCT Evidence in LLD
- Exercise may be a useful *second line* adjunct to medication
- Exercise has the potential to:
  - improve mood in the short term &
  - stimulate long-terms antidepressant mechanisms, such as neurogenesis

Journal of Affective Disorders 230 (2018) 65–70

ELECTROCONVULSIVE THERAPY (ECT)

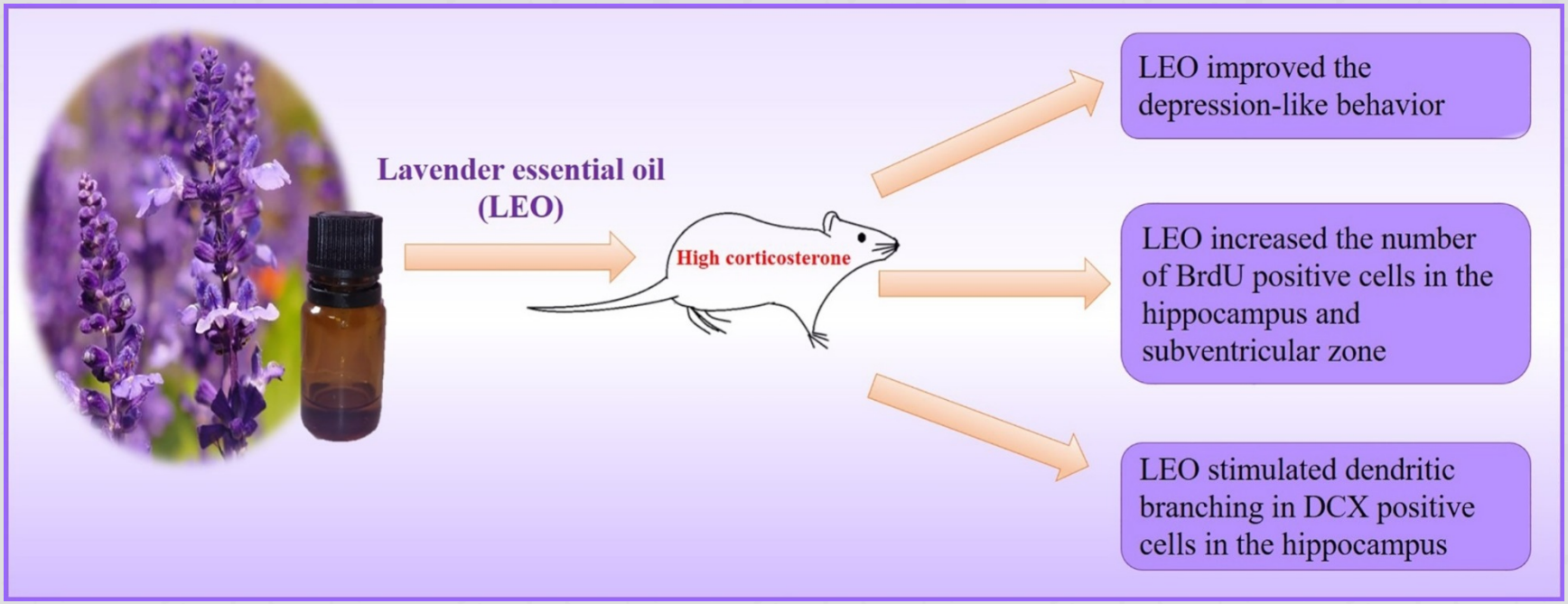
- Very effective modality of tx
- May work when other tx is ineffective
- Particularly helpful with psychotic features

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS)

- RCT evidence for efficacy in LLD
- N=52 age 60-85 yrs
- Remission rate was 40.0% for rTMS and 14.8% for sham rTMS
- NNT of 4
- well tolerated; pain was the only adverse effect more common with active rTMS

Kaster TS. Neuropsychopharmacology; 2018: 43:2231–2238;

(?) ESSENTIAL OILS/OXYTOCIN



Isabel SVD. Neuroscience Letters 701 (2019) 180–192

KETAMINE

- Pilot study evidence in treatment resistant LLD
- Ketamine increases synaptic connections & reverses depressive-like behavior in animal models,
- This supports the theory that ***synaptic loss*** contributes to depressive symptoms resistant to conventional antidepressants.

Duncan G.Am J Geriatr Psychiatry 25:11, November 2017
Holmes S.E. NATURE COMMUNICATIONS 2019;10:1529

AUDIENCE Q'S

- What is the typical improvement seen with antidepressant medication?
- What serious adverse events may be seen with SSRI's?
- What alternative interventions have evidence for efficacy?

AUDIENCE Q'S

- What is the typical improvement seen with antidepressant medication?
- ***average is ≈ 1.9-2.7 pts on HDRS***
- What serious adverse events may be seen with SSRI's?

- What alternative interventions have evidence for efficacy?

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- ***falls, fractures, bleeding, hyponatremia***
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- ***average is ≈ 1.9-2.7 pts on HDRS***
- What serious adverse events may be seen with SSRI's?
- ***falls, fractures, bleeding, hyponatremia***
- What alternative interventions have evidence for efficacy?
- ***CBT, exercise, bright light, socializing***

  (? rTMS & ketamine)

AUDIENCE Q'S

- Which drugs have evidence in late life depression?
- Which drug might work faster?

AUDIENCE Q'S

- Which drugs have evidence in late life depression?
- ***sertraline, duloxetine, fluoxetine, paroxetine, citalopram*** (*? vortioxetine , agomelatine)*
- Which drug might work faster?

AUDIENCE Q'S

- Which drugs have evidence in late life depression?
- ***sertraline, duloxetine, fluoxetine, paroxetine, citalopram*** (? vortioxetine , agomelatine)
- Which drug might work faster?
- ***mirtazapine***

WHAT I DO

- Recommend behavioral activation, increased socializing and exercise
- Encourage exposure to bright light
- If required, consider sertraline **(✔)** and mirtazapine (no specific evidence in LLD)

ANTIDEPRESSANT TAKE HOME POINTS

- Consider non-pharmacologic modalities
- Avoid anticholinergic antidepressants
- Avoid high doses
- Check sodium in 10-14 days (to rule out ↓)
- Monitor QTc on ECG (for ↑)
- Monitor for risk of bleeding
- *Watch for possible increased suicidality*
- Think about bone fragility fractures

ANXIETY

AUDIENCE Q'S

- What does the American Geriatrics Society recommend regarding benzodiazepines?
- What is the hip fracture risk in benzodiazepine vs antidepressant users?
- What agents have evidence for late life anxiety (GAD & Panic Disorder)?

ANXIETY DISORDERS

- Most anxiety disorders develop *between childhood and young adulthood*
- Generalized anxiety disorder (GAD) and agoraphobia have a relatively later onset .
- ≈50% of older patients with GAD report the onset of their disorder *after age 50*
- Late-life anxiety disorders are significantly associated with comorbid major depression.

Andreescu C & Lee S. *Anxiety Disorders*, Adv. Exp Medicine & Biology 2020

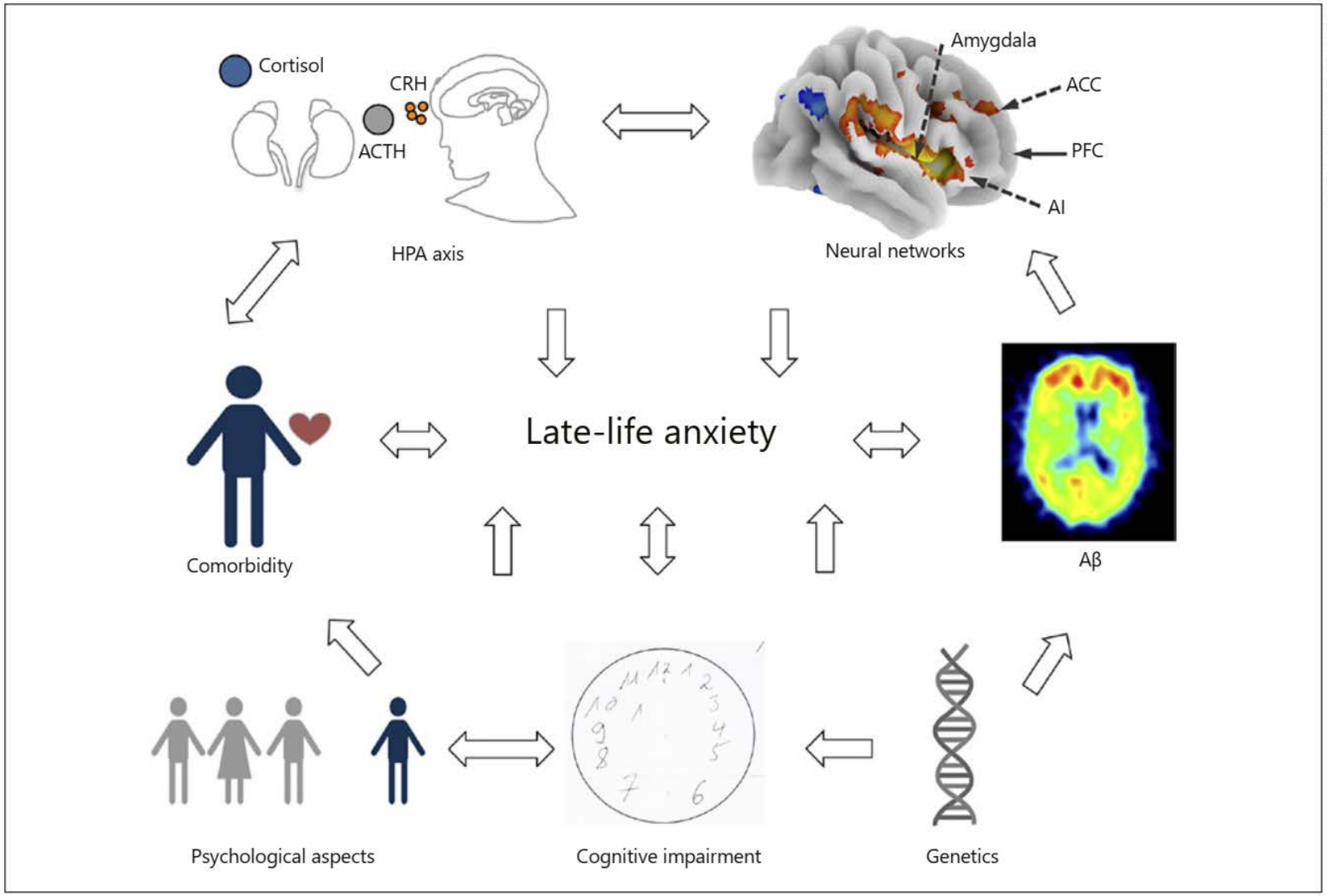

Fig. 1. Mechanistic model of anxiety in late life. ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone. For details, please refer to "Pathomechanisms of Anxiety in Late Life".

ANXIETY DISORDER PREVALENCE

- Estimates range from 1.2 to 15%.
- agoraphobia (4.9%),
- panic disorder (3.8%),
- generalized anxiety disorder (GAD) (3.1%),
- specific phobias (2.9%),
- social phobia (1.3%).

Hellwig S. Gerontology 2019;65:465–473

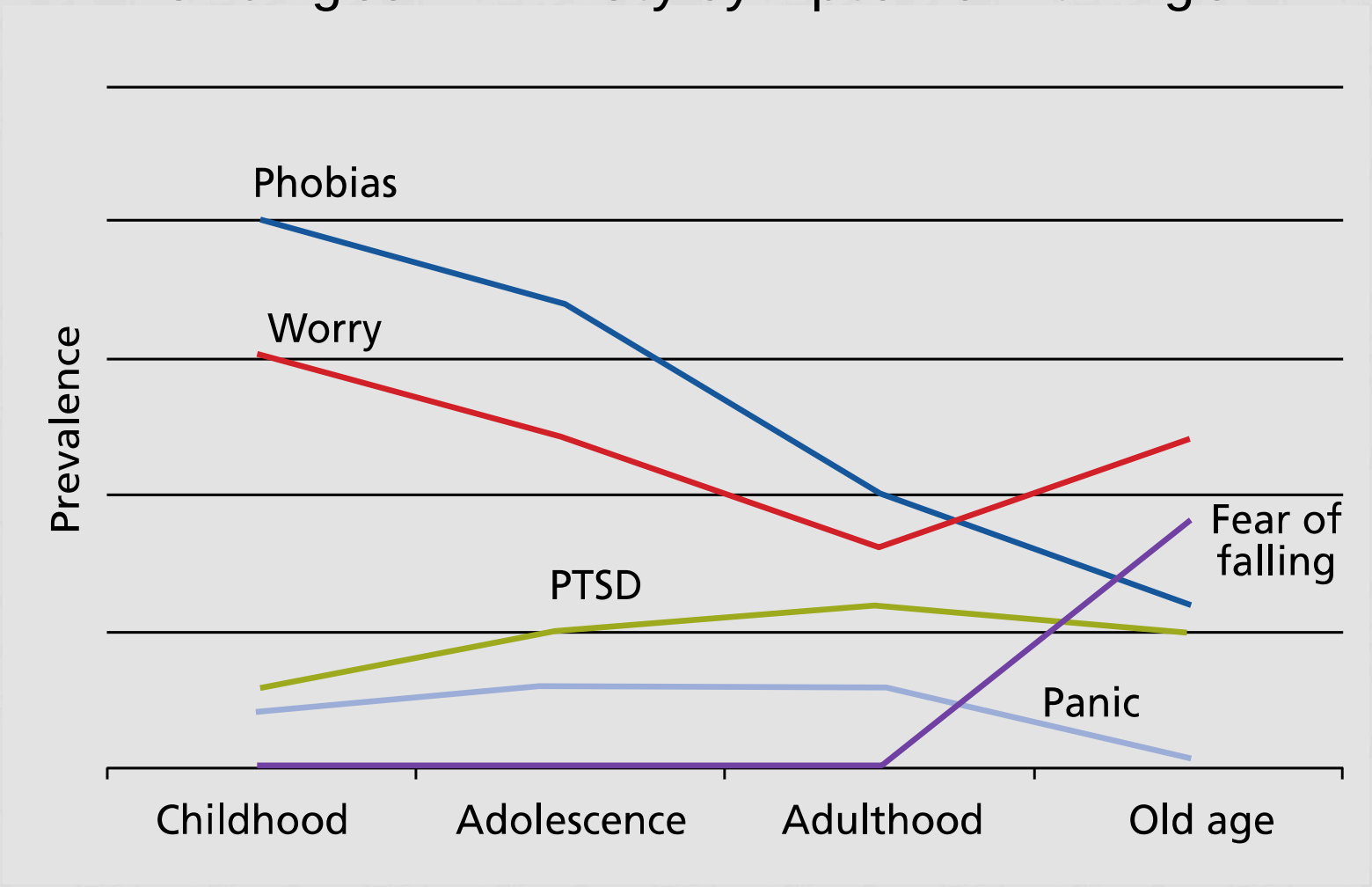

Figure 1. Changes in anxiety disorder presentation across the lifespan. PTSD, post-traumatic stress disorder

TX OF ANXIETY DISORDERS

- First-line treatment of late life anxiety disorders include:
  - psychotherapy, mostly cognitive behavioral therapy (CBT).
  - pharmacological treatment with SSRI's, & SNRI's
  - pregabalin in GAD

Wolitzky-Taylor KB.Depress Anxiety. 2010 Feb;27(2):190–211.
Hellwig S. Gerontology 2019;65:465–473

GENERALIZED ANXIETY DISORDER (GAD)

- Only 20% of older adults with severe worry meet GAD criteria[1]
- Most studies in older adults have been on ***GAD*** [2]
- Drug studies in people > 65 show they respond to treatment similarly to those aged < 65 [2]

[1]Golden J, et al. Aging Ment Health. 2011;15(8):985–94
[2] McMaster PBSG EDUCATIONAL MODULE Vol. 22 (2), February 2014

DSM5 GAD **Diagnostic Criteria**

- **Excessive anxiety and worry** for ≥ 6 months,
- The individual finds it difficult to control the worry.
- ≥ 3 of the following :
  - **Restlessness**.
  - **Fatigue.**
  - **Difficulty concentrating**.
  - **Irritability.**
  - **Muscle tension**.
  - **Sleep disturbance**
- The anxiety or worry causes distress or impairment in functioning.

DRUG TX OF ANXIETY IN LATE LIFE

- For GAD and Panic D/O in older populations, there is evidence for:
  - citalopram[1]
  - escitalopram[2]
  - venlafaxine ER[3]
  - duloxetine[4]
  - sertraline[5]
  - buspirone[5]
  - pregabalin (GAD)[6]

[1]Lenze EJ. Am J Psychiatry. 2005;162(1):146–50. [2] Lenze EJ. JAMA. 2009;301(3):295–303.
[3] Katz IR. J Am Geriatr Soc. 2002;50(1):18–25. [4] Davidson J. Psychopharmacol. 2008;23(6):519–26. [5] Mokhber N et al. Psychiatry Clin Neurosci. 2010;64:128-133 [6] Montgomery S. Br J Psych 2008;193(5):389-94

DRUG TX OF ANXIETY IN LATE LIFE

- There is also RCT evidence in late life GAD for:
  - quetiapine

Mezhebovsky I. Int J Geriatr Psychiatry 2013; 28: 615–625.

CBT-TELEPHONE (CBT-T)

- CBT-T circumvents major obstacles to effective treatment of late-life anxiety:
  - limited access due to mobility issues
  - agoraphobia prevents patients from leaving their home
  - privacy accommodates the needs of older adults with an anxiety disorder

Hellwig S. Gerontology 2019;65:465–473

EVIDENCE BASED TX ANXIETY

- There is some evidence that older adults can also benefit from internet-based CBT.
  - ***e.g MindShift***
  - http://www.anxietycanada.ca/

BENZODIAZEPINES

- The American Geriatrics Society recommends ***avoiding*** **benzodiazepines** in those > 65 yrs of age .

Pary R. POSTGRADUATE MEDICINE 2019, VOL. 131, NO. 5, 330–332

BENZODIAZEPINES

- Benzodiazepines, and Z-drugs are significantly associated with an ↑'d risk of hip fracture
- (BZ RR = **1.52**, 95% CI 1.37–1.68)
- (Z drugs RR = **1.90**, 95% CI 1.68 – 2.13)

Donnelly K, et al PLoS ONE (2017) 12(4): e0174730.

BUT ARE SSRI'S SAFER?

- Relative risk (RR) of fractures with SSRI use in elderly patients is similar to BZ's:
  - (RR) = **1.60** (95% CI 1.38 - 1.86)

(?)FASTING

- The production of **ketone bodies** appears to lead to enhancement of mood and neuroprotection.
- Amin et al. found reduced depression and anxiety scores after Ramadan fasting.

Ika Fidianingsih J of Comp and Integ Medicine. 2019; 20170172

(?)CBD

- Cannabinoids appear to demonstrate *moderate efficacy* in pain and chemotherapy-related nausea;
- There are limited data to suggest benefits in the treatment of anxiety

Beedham W. Geriatrics 2020, 5, 2; doi:10.3390/geriatrics5010002

AUDIENCE Q'S

- What does the American Geriatrics Society recommend regarding benzodiazepines?
- What is the relative risk of hip fracture in benzodiazepine vs SSRI users?

AUDIENCE Q'S

- What does the American Geriatrics Society recommend regarding benzodiazepines?
  - **avoid benzodiazepines in people > 65**
- What is the relative risk of hip fracture in benzodiazepine vs SSRI users?

AUDIENCE Q'S

- What does the American Geriatrics Society recommend regarding benzodiazepines?
  - **avoid benzodiazepines in people > 65** .
- What is the relative risk of hip fracture in benzodiazepine vs SSRI users?
  - RR BZ = **1.52** vs. RR SSRI = **1.60**

AUDIENCE Q'S

- What agents have evidence for late life anxiety (GAD & Panic Disorder)?

AUDIENCE Q'S

- What agents have evidence for late life anxiety (GAD & Panic Disorder)?
  - citalopram
  - escitalopram
  - sertraline
  - venlafaxine ER
  - duloxetine
  - pregabalin
  - buspirone

WHAT I DO

- If MMSE ≥ 27, consider CBT or psychotherapy
- Consider ***mirtazapine*** (start 7.5-15 mg at HS)
- Occasionally use:
  - ***quetiapine***
    - (RCT dose was168 mg daily)
  - ***pregabalin***
    - (RCT dose was 270 mg daily) but lowest effective dose is best

CASE: VC

- 82 yof with anxiety, depression & c/o poor sleep
- D-E-P-R-E-S-C-R-I-B-E
- Recommend ***reducing citalopram***, ↓ and ***d/c zopiclone***
- Aim for ***zero lorazepam***
- Encourage *behavioral activation*
- Consider alt pharmacotherapy if req

KEY CONCEPTS

- Optimal brain health depends on cellular renewal
- The brain has a ***novelty & calorie-centric*** design
- *Observing these principles brings automatic benefits*
- The modest benefits of antidepressants is an indication we must address these other factors

Mattson MP. Trends in Cognitive Sciences, March 2019, Vol. 23, No. 3

STRATEGIES PROMOTING BRAIN HEALTH

- Treat hypertension
- Maintain low BMI in middle age
- Avoid hyperglycemia (↓ insulin resistance)
- Prescribe physical exercise
- Social activity
- New challenges (eustress)
- Sufficient deep sleep

should be promoted as critical factors in brain health

Nehls Journal of Molecular Psychiatry (2016) 4:3

Q's

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