Severe mental illness and dementia

this content is up-to-date as of May 3, 2021
Learning objectives

• appreciate the increased risk of dementia in persons with schizophrenia, bipolar disorder, major depressive disorder and substance use disorder

• describe the relationship between psychototropic medications and dementia
Chronic mental illness & risk of dementia

- schizophrenia
- bipolar disorder
- major depressive disorder
- alcohol
- medications
Schizophrenia (1)

- people with schizophrenia have roughly twice the risk of developing dementia as those without (RR* = 2.29)¹
- they may develop dementia earlier²:
  - by age 65: 1.8% had dementia (vs 0.6% for people w/o schizophrenia)
  - by age 80: 7.5% (vs 5.8%)

¹Cai & Huang, *Neuropsychiatr Dis Treat* 2018; ²Ribe et al., *JAMA Psychiatry* 2015; * RR = relative risk
Schizophrenia (2)

• why?
  • tobacco $\rightarrow$ vascular disease
  • other medical comorbidities (diabetes, heart disease)
  • alcohol & other substances
  • low physical activity
  • poor access to medical care (?)
  • lower cognitive reserve (?)
  • shared genetic risk (?)
Bipolar disorder

- people with bipolar disorder have roughly twice the risk of developing dementia as those without (OR*=2.36)

- why?
  - tobacco, alcohol & other substances
  - medical comorbidities (obesity, diabetes, sleep apnea)
  - risky behaviors
  - diet & exercise
  - neuroinflammation & decreased neuroplasticity
  - unclear if number of episodes correlated with dementia

Diniz et al., Am J Geriatr Psychiatry 2017; * OR = odds ratio
Major depressive disorder (1)

- people with MDD have roughly twice the risk of developing dementia as those without (OR* either 1.90 or 2.03, depending on type of study)
- risk of vascular dementia (2.52) slightly higher than risk of Alzheimer’s disease (1.65)
- late-onset depression may represent prodrome of dementia
- contradictory evidence regarding whether early-onset or late-onset depression confers greater risk
- depression increases risk of progression from MCI to dementia

Ownby et al., Arch Gen Psychiatry 2006; Diniz et al., Am J Geriatr Psych 2013; Walaszek, Late-Life Depression & Anxiety, submitted. * OR = odds ratio
Major depressive disorder (2)

- why?
  - neuroinflammation
  - chronic HPA axis activation
  - dysfunctional neural networks
  - tobacco, alcohol
  - diet & exercise
  - shared risk: genetics, social determinants of health, chronic medical problems
Alcohol & risk of dementia

- in general, studies have shown that light alcohol use may reduce risk of dementia
- high alcohol use increases risk of dementia and results in smaller hippocampi

10 units = five 12-oz beers

Sabia et al., *BMJ* 2018; Topiwala et al, *BMJ* 2017
Medications & risk of dementia

- lithium\(^1\): may be neuroprotective and reduce risk of dementia
- valproic acid\(^2\): in people with dementia, may increase the rate of shrinkage of the brain
- anticholinergic medications\(^3\): can cause reversible cognitive impairment in people with schizophrenia \(\geq 50\) years old
- benzodiazepines\(^4\): conflicting evidence about risk of dementia; do cause reversible cognitive impairment
- antipsychotics: ?

\(^1\)Diniz et al., *Neuropsychiatr Dis Treat* 2013; \(^2\)Tariot et al., *Arch Gen Psychiatry* 2011; \(^3\)Tsoutsoulas et al., *J Clin Psychiatry* 2017; \(^4\)Grossi et al., *BMC Geriatr* 2019
Psychotropic medications on the Beers list

**Potentially inappropriate**

- antidepressants
  - ami-/nortriptyline
  - clomipramine
  - desi-/imipramine
  - doxepin > 6 mg/d
  - paroxetine
- all antipsychotics
- all benzodiazepines
- z-drugs
- also: other medications with anticholinergic effects

**Use with caution**

- antipsychotics
- carbamazepine/oxcarbazepine
- SSRIs
- SNRIs
- mirtazapine
- TCAs
- dextromethorphan-quinidine

**Drug-drug interactions**

- lithium
- and others
What to do about psychotropic medications

- consider dose reduction or discontinuation of medications for pre-existing mental illness, especially valproate, benzodiazepines, anticholinergics, antipsychotics
- consider cognitive enhancer to delay progression of dementia
- use medications for BPSD only if imminent dangerousness or severe distress (start low, go slow)