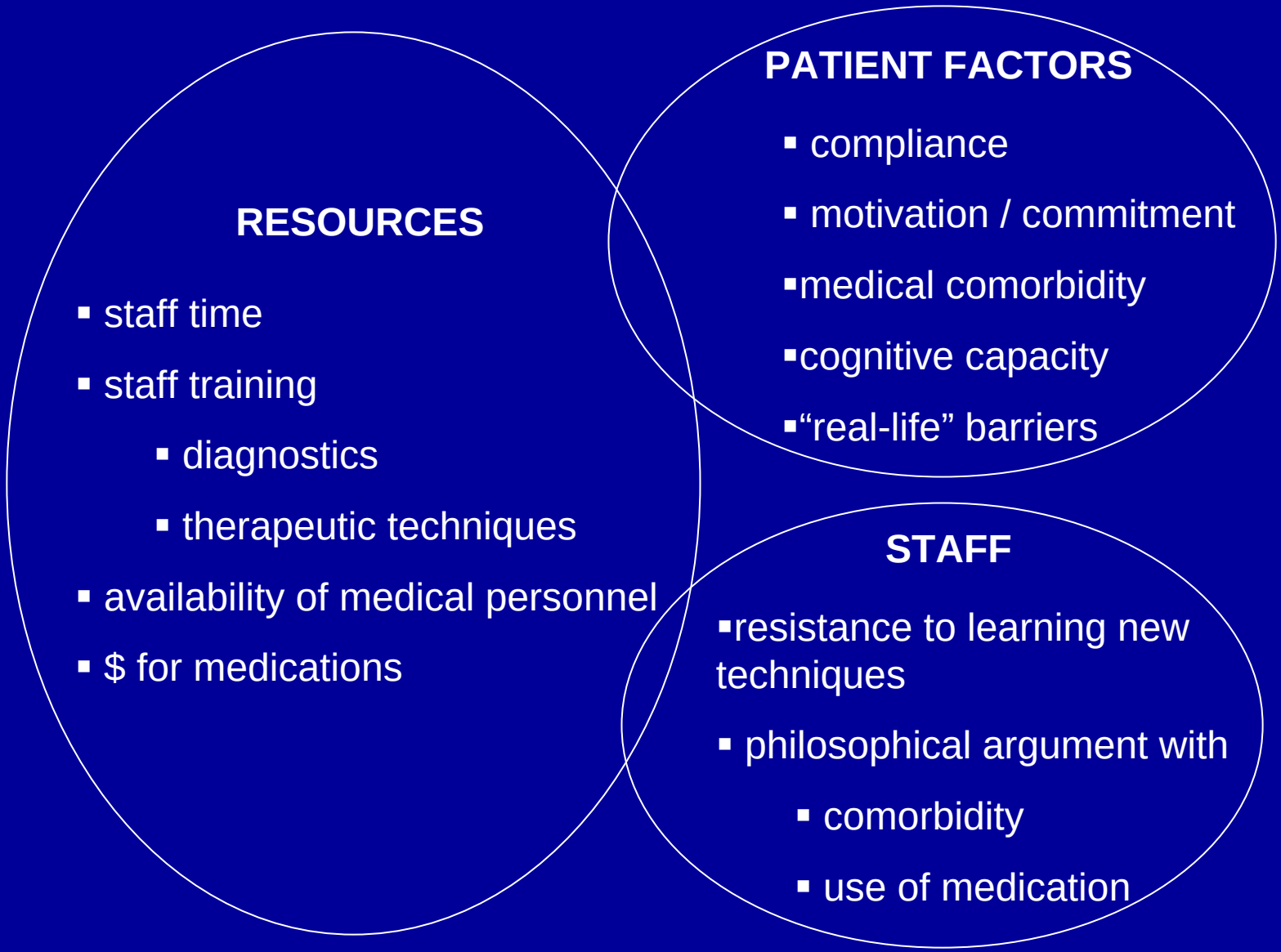
Evidence-Based Treatments for Comorbid Substance Use and Psychiatric Disorders:

What are they and why aren't we using them???

Problems in Implementing Evidence-Based Practice



Exploring with Drugs

Before

…..And After

Problems with Pharmacotherapy

- Complex biopsychosocial disorder - no “magic bullet”
- Enhanced risks of toxicity
  - Medical comorbidities
  - Overdose
  - Combination with drugs of abuse
- Philosophy of treatment
- Passive-dependent role

Psychotherapy

- Important to maximize non-pharmacologic strategies
  - Enhance self-efficacy
  - Decrease helplessness/dependency
  - Enhance coping strategies

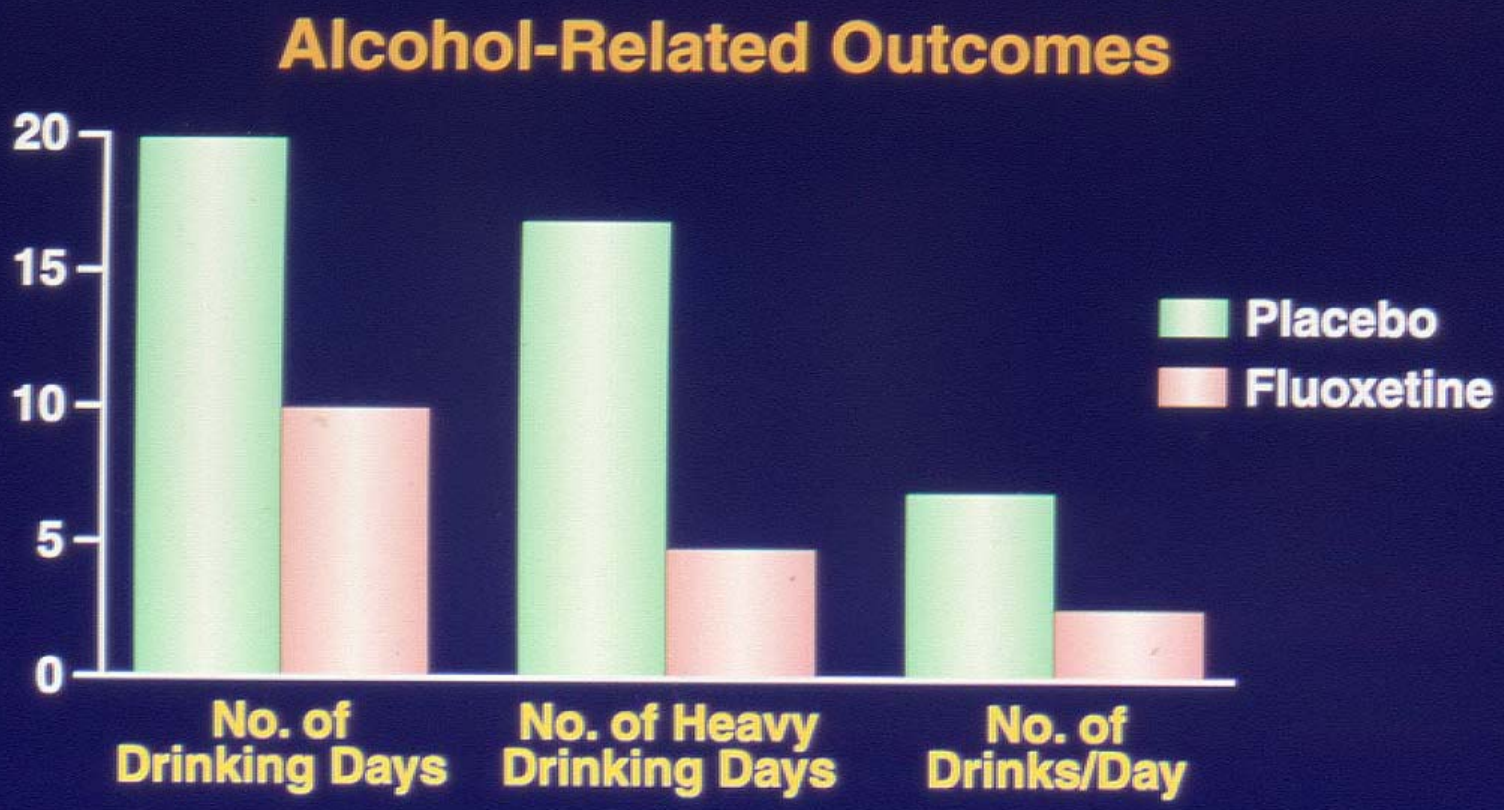
Anti-depressants in Depression and Substance Use Disorders

	Tricyclics		SRI's		Other
	Sub Use	Mood	Sub Use	Mood	
Nicotine	++	++	-	+	Buproprion ++
Alcohol	+	++	++	++	Nefazadone -
Cocaine	+	+	-	-	
Opiates	+	+	-	-	

Fluoxetine in Alcoholics with MDE

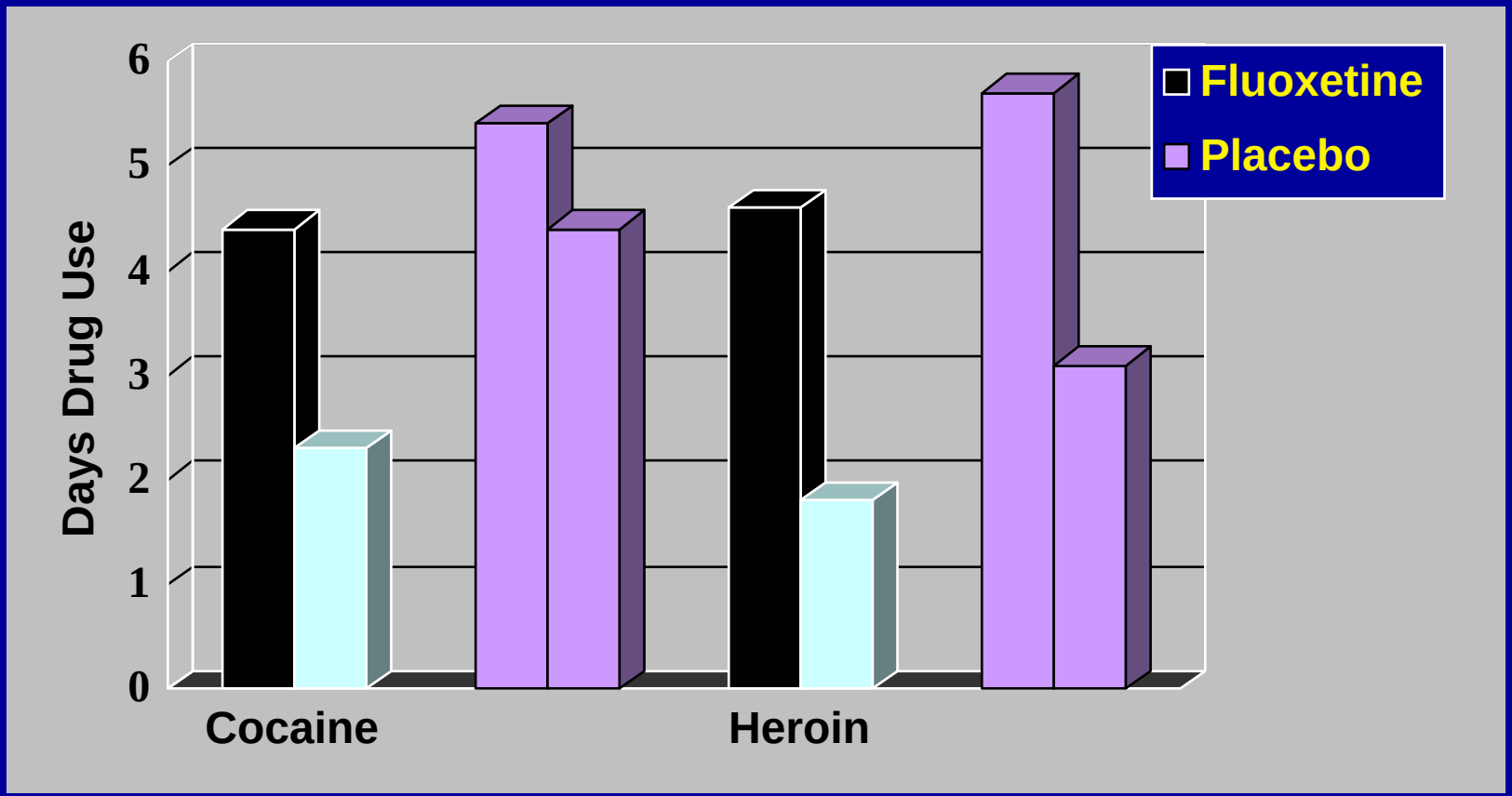
- Double-blind, placebo-controlled trial
- 12 week study (N=40)
- Both alcohol and depression outcomes monitored
  - » Cornelius et al., 1996

Fluoxetine in Depressed Alcoholics



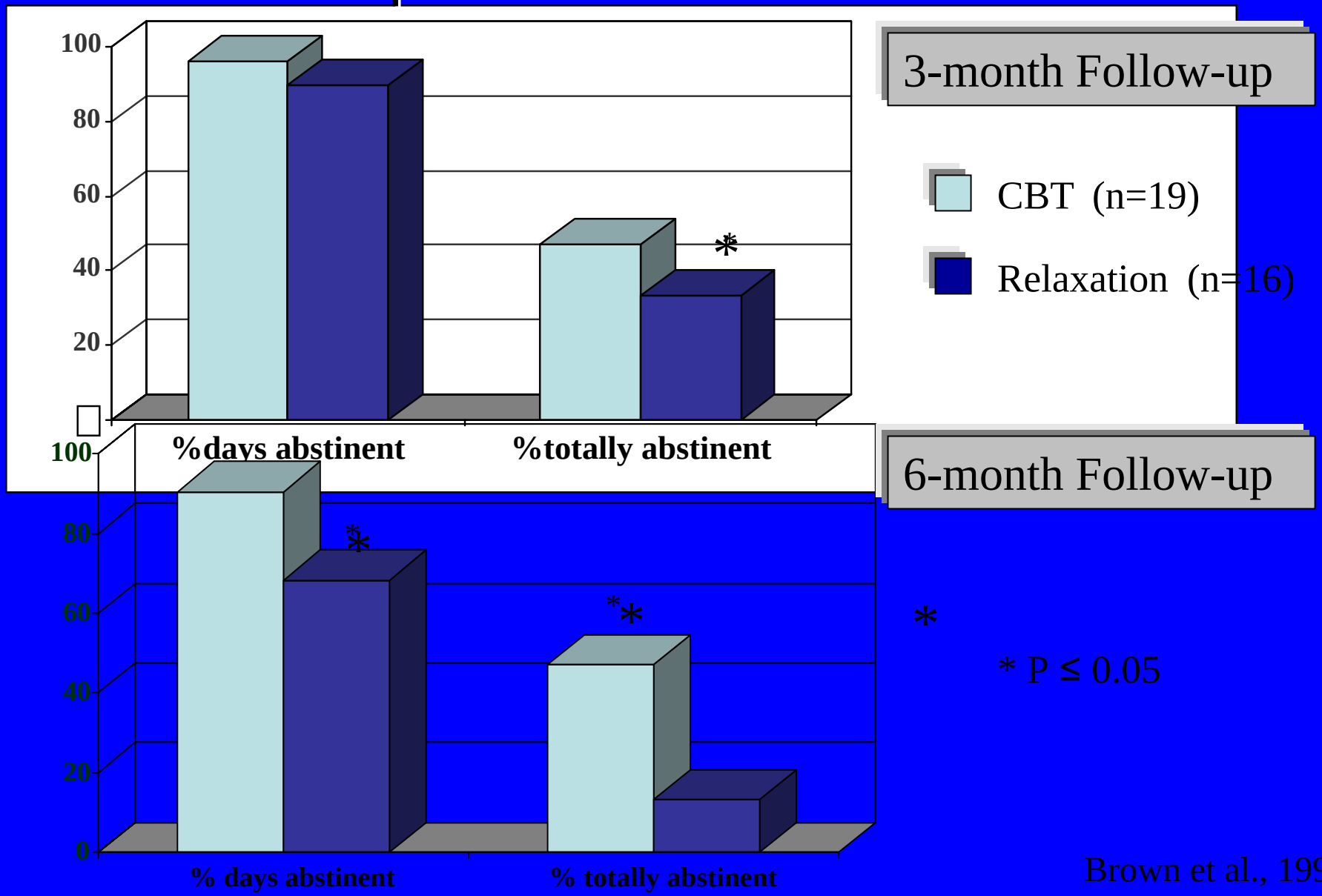
Cornelius et al, 1997

Fluoxetine in Depressed Methadone-Maintained Patients



Petrakis et al, 1998

Cognitive Behavioral Treatment for Depression in Alcoholism



Brown et al., 1997

Treatment of Depression with Alcohol/Drug Dependence

- Antidepressants effective in treatment of depression (?TCA's > SSRI's)
- Improvement in depression - decrease substance use
- Use of evidence based psychotherapy important
- Abstinent period before diagnosis/trt
  - » Nunes and Levin, 2004, JAMA

PTSD Integrated Treatment

- Triffleman et al (1999) - manualized individual therapy: relapse prevention + stress inoculation + in vivo exposure
- Najavits et al (1996) - “Seeking Safety” manualized group therapy: relapse prevention, education, affect management
- Brady et al (1998) - manualized individual therapy: imaginal exposure + relapse prevention

Seeking Safety

- 24 sessions in 12 weeks
- Group therapy integrating CBT for substance use disorders and PTSD
- Emphasis on safety, anxiety management, interpersonal relationships - no exposure

Seeking Safety

- Best studied intervention
- Six trials on-going
- Controlled trial demonstrated equivalent efficacy to relapse prevention therapy, both superior to treatment as usual

» Hein et al., Am J. Psychiatry, 2004


ALL MY FRIENDS THINK I'M CRAZY
WHY DON'T YOU KILL THEM ?

Exposure Therapy in PTSD/Cocaine Dependence

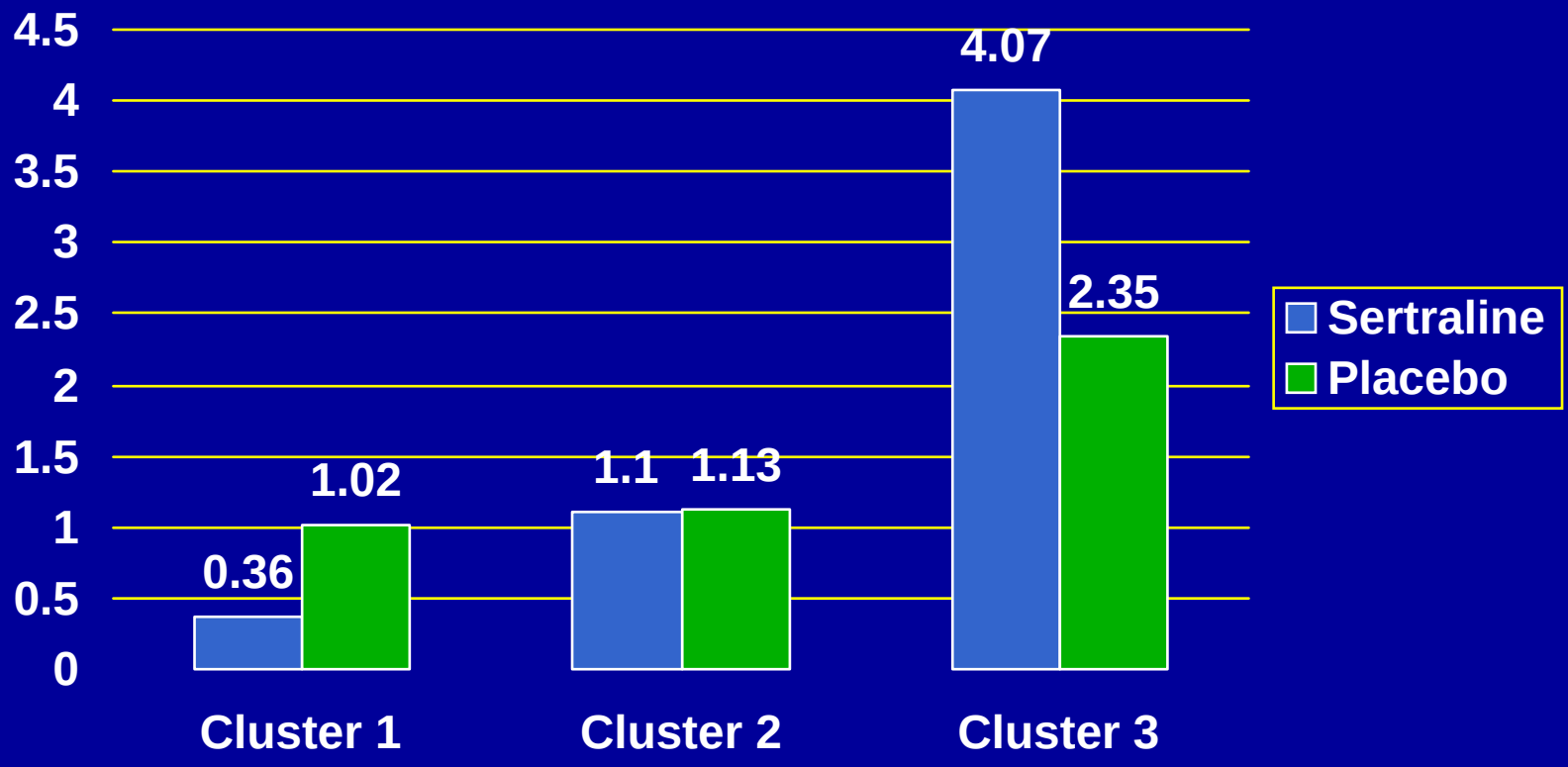
- 16 sessions, manual guided, individual therapy
- First 6 sessions CBT for cocaine - education re: trauma response/ PTSD
- Sessions 7-14 exposure

Brady et al., 2001

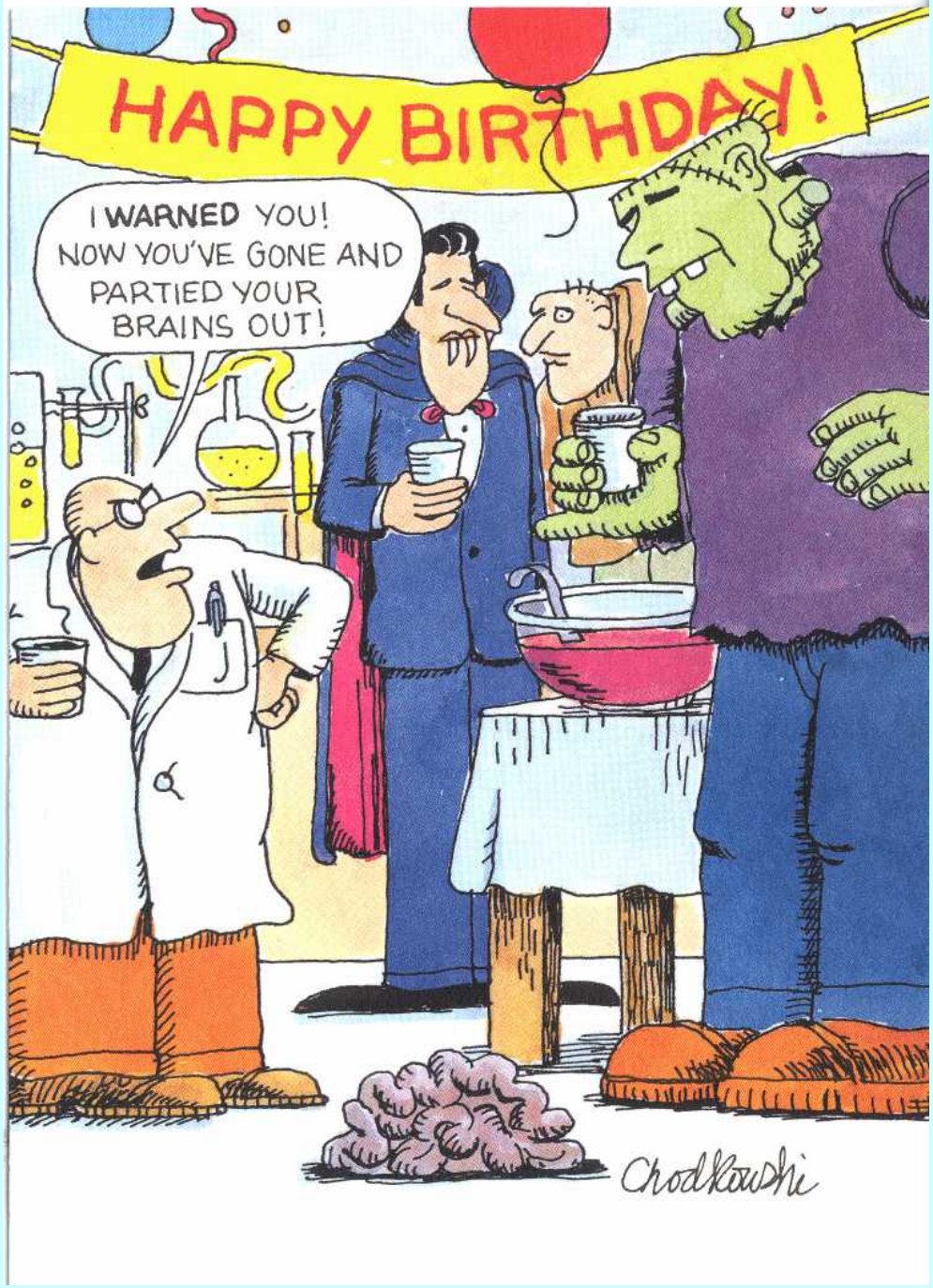
PTSD / Alcoholism: Treatment with Sertraline

- 12 week study
- Double blind/placebo controlled trial
- Weekly CBT targeting alcoholism
- Measure alcohol and PTSD outcomes
- 112 subjects with both PTSD/alcoholism
  - 62 women; 50 men

Adjusted Mean Average Days Drinking Over Treatment Period



Cluster x group p=0.068


HAPPY BIRTHDAY!
I WARNED YOU! NOW YOU'VE GONE AND PARTIED YOUR BRAINS OUT!
Chodkowski

Bipolar Disorder and Kindling

Reactive Episodes

↓

Spontaneous Episodes

↓

↑ Frequency, ↑ Severity

↓

Rapid Cycling

↓

Continuous Cycling

↓

Treatment Refractoriness

Alcohol and Neuronal Loss

- Neuroadaptive changes result in excitotoxic damage
- Preclinical models:
  - Ethanol-induced loss of pyramidal neurons & dentate granule cells
  - Exacerbated loss of neurons by alcohol withdrawal
- Clinical models:
  - Increased markers of oxidative stress in CSF
  - Decreased gray & white matter volume

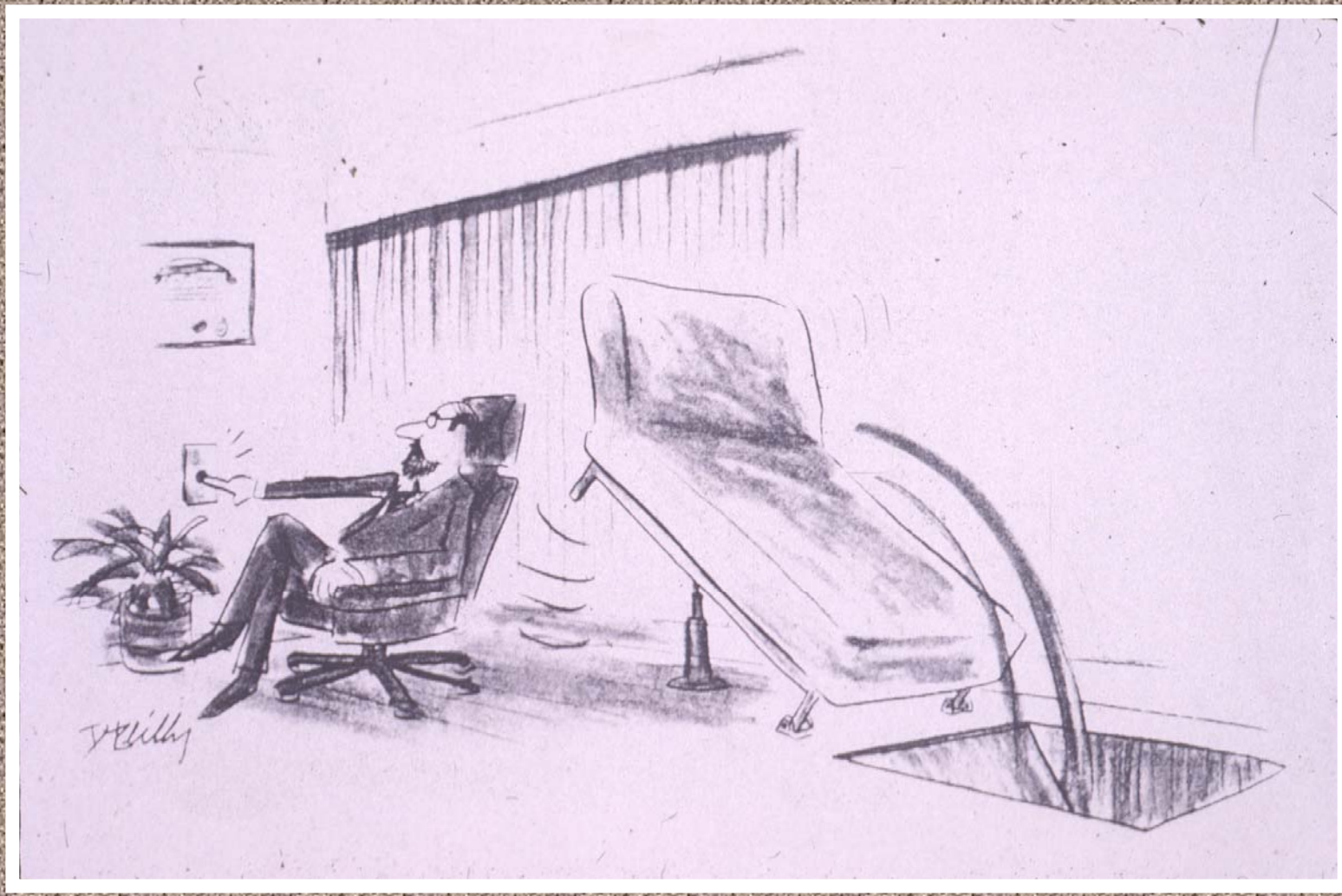
Neuroprotection?

- Repeated episodes of withdrawal could worsen neuronal damage
- Plausible neuroprotective and neurotrophic potential of mood stabilizers
  - antiapoptotic, antitoxic, and neuroprotective effects important in alcoholism
- Suggests possibility of disease modification

Valproate in Bipolar Alcoholics

- Double-blind, placebo-controlled
- N=52
- DVPX+TAU vs PBO+TAU
- TAU=lithium and psychosocial treatment
- Results
  - DVPX group had decrease heavy drinking days
  - DVPX group had less “any” drinking days
  - Both groups had decrease in affective symptoms

Salloum et al, Archives General Psychiatry, in press



Psychotherapy in Substance-Using Bipolar Patients

- Cognitive behavioral therapies effective in both disorders
- Development of specific “integrated” therapy
  - topics relevant to both disorders
  - relationship of disorders
- Integrated Group Therapy had better outcomes
  - ASI scores
  - % months abstinent

Weiss et al., 2000

Integrated Treatment of Comorbidity

- Medical approach should not replace public policy/ environmental-directed change
  - Housing in drug-free neighborhoods
  - Social/educational/voactional opportunities
  - Same positive/protective factors operational
  - New developments can only be implemented if treatment system is intact
    - » Drake et al., 2004

General Principles in Treatment of Comorbidity

- Address both problems simultaneously
- Use medication with least abuse potential and least toxicity should relapse occur
- Maximize the use of non-pharmacologic treatment
- When possible, use medications which treat both disorders