TREATMENT-RESISTANT DEPRESSION AND ANXIETY

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Definition of treatment resistance

- Failure to remit after 2 adequate trials of medication
- Includes remitters who relapse within a certain period of time
Determining treatment-resistance

- Wrong diagnosis
- Inadequate treatment
- Treatment intolerance
- True treatment resistance
Diagnostic issues

- **Psychiatric**
  - Unipolar vs. bipolar depression
  - Elevated rates of anxiety disorders in bipolar illness

- **Medical**
  - Sleep apnea
  - Thyroid dysfunction

- **Substance**
  - Illicits
  - Prescriptions: steroids, opioids, benzos
Treatment adequacy

- DOSE of Medication
- DURATION of Medication
- TYPE of Medication – drug mechanism of action
Adequacy of antidepressant treatment

SSRIs:
- Citalopram 20mg
- Escitalopram 10mg
- Fluoxetine 20mg
- Paroxetine 20mg
- Sertraline 100 mg

SNRIs:
- Venlafaxine 150mg
- Bupropion 300mg
- Duloxetine 60mg
- Mirtazapine 30mg

TCAs:
- Nortriptyline 75mg
- Amitriptyline 200mg
- Desipramine 200mg

- Minimal treatment duration: 4 weeks

(Recommendations from D. Dunner)
Assuring appropriate type of medication

- Benzos do not work for PTSD
- TCAs do not work for social phobia
- Buspirone and Trazodone work ONLY for GAD
- Propranolol works only for performance anxiety
- Bupropion does not work for any anxiety disorder
Treatment intolerance and non-adherence

- Hypersensitivity to medications (especially in patients with high anxiety and panic)
- Negative beliefs about treatment efficacy (negative placebo response; more frequent treatment dropout)
- Recovery and acute illness model (late non-adherence)
- Fear of medication “dependence” (sometimes confused also with fears of medication “addiction”)
- Prior adverse personal or familial experiences with medication
- Structural and other barriers to treatments—low income, culture and ethnicity
Approaches to treatment intolerance

- Education and patient preparation (explanatory model, past experience, time course)
- Close monitoring for first few weeks
- Exposure with low dose, slow titration
- Side effects reframing consistent with patients own model of illness
Treatment resistance: key factors

- Exogenous factors
- Comorbidity
- Unimodal treatment
Treatment resistance: Exogenous factors

- **Health Habits**
  - Caffeine
  - Alcohol
  - OTC cold preparations
  - Nicotine (panic risk)
  - Lack of exercise/Deconditioning
  - Sleep Deprivation
  - Irregular sleep-wake cycle

- **Life Events/Stress**
  - Acute
  - Chronic (low SES; lack of social support)

- **Substance Abuse**
  - Marijuana
  - Cocaine
  - Alcohol
Effect of psychosocial stressors on treatment response

- Disturbed spouse and family relationships predict lack of remission in GAD (Yonkers et al, 2000)
- Chronic life stressors (interpersonal, danger, loss) diminish effect of anti-panic treatment (Wade et al, 1993)
- Poorer SSRI response in low income patients (Roy-Byrne et al, 2003)
- Poorer social support and more life events predict PTSD chronicity (Udwin et al, 2001)
Exercise is good for depression and anxiety

- Exercise is effective for mild to moderate depression (90 articles; Herring et al 2012)
- Exercise reduces cholecystokinin-induced panic (Stroehle et al 2005)
- Exercise is superior to placebo in reducing panic attacks and equal to medication in reducing anticipatory anxiety (Brooks et al, 1998)
Treatment resistance: Comorbidity

- Major depression (especially recurrent, more severe)
- Anxiety disorders (especially various phobias)
- Personality Disorder
  - Acute and long-term poor outcome predictor
- Substance Abuse
  - Greatest effects on treatment engagement
  - Alcohol also predicts poor outcome in engaged patients
Treatment resistance: Unimodal treatment

- Underutilization of evidence-based psychotherapy, such as CBT
- Non-MD therapists may delay medication until therapy has failed--now patient is biased against therapy
Combining 2 antidepressants with complimentary mechanism of action or side effect profile
- eg., SSRI + bupropion, SSRI + TCA

Atypical antipsychotics
- Use lower than antipsychotic dose, 6-8 week trial, discontinue if ineffective
  - aripiprazole 10-15mg, olanzapine 5-10mg, risperidone 0.5-1mg, ziprasidone 60-80mg

Lithium 600-900mg

Liothyronine (Cytomel) 12.5-25mcg
Treatment-resistance depression: Other approaches

- ECT
  - Usually quick response
  - Needs maintenance medication to prevent relapse

- MAO Inhibitors
  - phenelzine 60mg
  - selegiline patch 6-12mg/24h
  - tranylcypromine 40mg
Treatment-resistance anxiety: Pharmacotherapy

- Start with antidepressant baseline (SSRI, venlafaxine or mirtazapine)
- Wait long enough for complete response
- Adjunctive treatments
  - Another antidepressant (esp. for panic disorder)
  - Atypical antipsychotic for GAD or PTSD
  - Anticonvulsant – pregabalin for GAD and social phobia, lamotrigine for PTSD, gabapentin for social phobia
  - Buspirone for social phobia
  - Prazosin for nightmares and hyperarousal in PTSD
- Simplify regimen after 6–12 months
Treatment-resistance anxiety: Psychological treatment

- CBT
- Imagery rehearsal
- Mindfulness exercises
Did we mention exercise?

“it’s not a rash, it’s moss. You need to start being more active than a tree.”