OCD & Anxiety:
Symptoms, Treatment, & How to Cope

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Outline of talk

- **Introduction**
  - ***Very* brief introduction to anxiety disorders**
  - ***Very* brief introduction to our OCD research program**
- **What do we know about OCD?**
  - What is it?
  - How do we treat it?
  - What causes it?
- **Opportunities and Challenges**

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- **Research support:**
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    - *Current: R01 MH045436 (PI: Simpson); R01 MH091694 (PI: Simpson, Schneier, Fyer); K24 MH091555 (PI; Simpson); R34 MH095502 (PI: Simpson, Rynn, Shungu); R21 MH093889 (PI: Simpson, Marsh)*
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    - Medication from Janssen Pharmaceutica for an NIMH-funded study (2006-2012)
    - Unrestricted gift from Neuropharm Ltd to explore novel medications in OCD (2009)

- **Scientific Advisory Board/Consultant:**
  - Jazz Pharmaceuticals (re. Luvox CR, 2007)
  - Pfizer (re. Lyrica, 2009)
  - Quintiles, Inc (re. therapeutic needs for OCD, 9/2012)

- **Other**
  - Royalties from UpToDate and Cambridge University Press

Anxiety Disorders

- Group of illnesses characterized by fear and/or anxiety:
  - Posttraumatic stress disorder
  - Obsessive-compulsive disorder (OCD)
  - Social anxiety disorder/Social phobia
  - Panic Disorder & Agoraphobia
  - Specific Phobia
  - Generalized anxiety disorder
- Prevalence: 29% of adults in America
- Onset: often childhood or adolescence (*precursor to depression*)
- Impact public health

Evidence-based treatments

- Medications
  - Serotonin reuptake inhibitors (e.g., Prozac, Zoloft)
  - Benzodiazepines (e.g., Ativan, Klonopin)

- Cognitive-behavioral therapy
  - Exposure to stimuli that generate anxiety
  - Modifying maladaptive cognitions

Overview of our OCD research program

- Clinical research: ***for patients of today***
  - Examining how best to combine pharmacotherapy and psychotherapy
  - Testing novel treatment strategies*

- Neurobiological research: ***for patients of tomorrow***
  - Studying brain circuits implicated in OCD (PET, MRS, fMRI)*
  - Identifying shared & distinct neural correlates of behavior across disorders
  - Examining brain mechanisms using animal models*

* BBRF/NARSAD supported pilot studies.

What is OCD?

OCD: A Disabling Disorder

- Lifetime Prevalence: ~2%
- Median age of onset = 19 (versus Major Depression=32)
  - 25% of cases by age 14
- Typically chronic, waxing and waning course
- High proportion of serious (50%) and moderate (35%) cases

Skoog and Skoog 1999; Kessler et al. 2005; Ruscio et al. 2008

Hallmarks of OCD

- ***Obsessions:*** repetitive thoughts, impulses, or images that are intrusive, inappropriate, and distressing

- ***Compulsions:*** repetitive behaviors or mental acts that the person performs to reduce distress or to prevent a feared outcome

- Symptoms are distressing, time consuming, and impairing.

Diagnostic and Statistical Manual of Mental Disorders

Clinical Phenotype

- Associated features
  - Range of content and fears (“symptom dimensions”)
    - *Harm, contamination, taboo thoughts, symmetry, hoarding*
  - Different affects
    - *Anxiety, tension/not just right, disgust*
  - Range of insight

- Comorbidity
  - Depressive and other anxiety disorders
  - Tics, Tourette’s Disorder, and ADHD
  - OC “spectrum:” eating disorders, trichotillomania, skin picking, BDD
  - Other: Schizophrenia, autism, bipolar disorder

What is not OCD?

- Intrusive thoughts and repetitive behaviors occur in all of us.

- Distinguishing OCD from other disorders
  - Obsessions versus worries (GAD) or ruminations (MDD)
  - OCD versus PTSD
  - OCD versus other disorders with repetitive behaviors (e.g., Trichotillomania or Skin Picking)
  - OCD versus Hoarding Disorder
  - OCD versus Obsessive-Compulsive Personality Disorder

How is OCD treated?

First-line Treatments for OCD

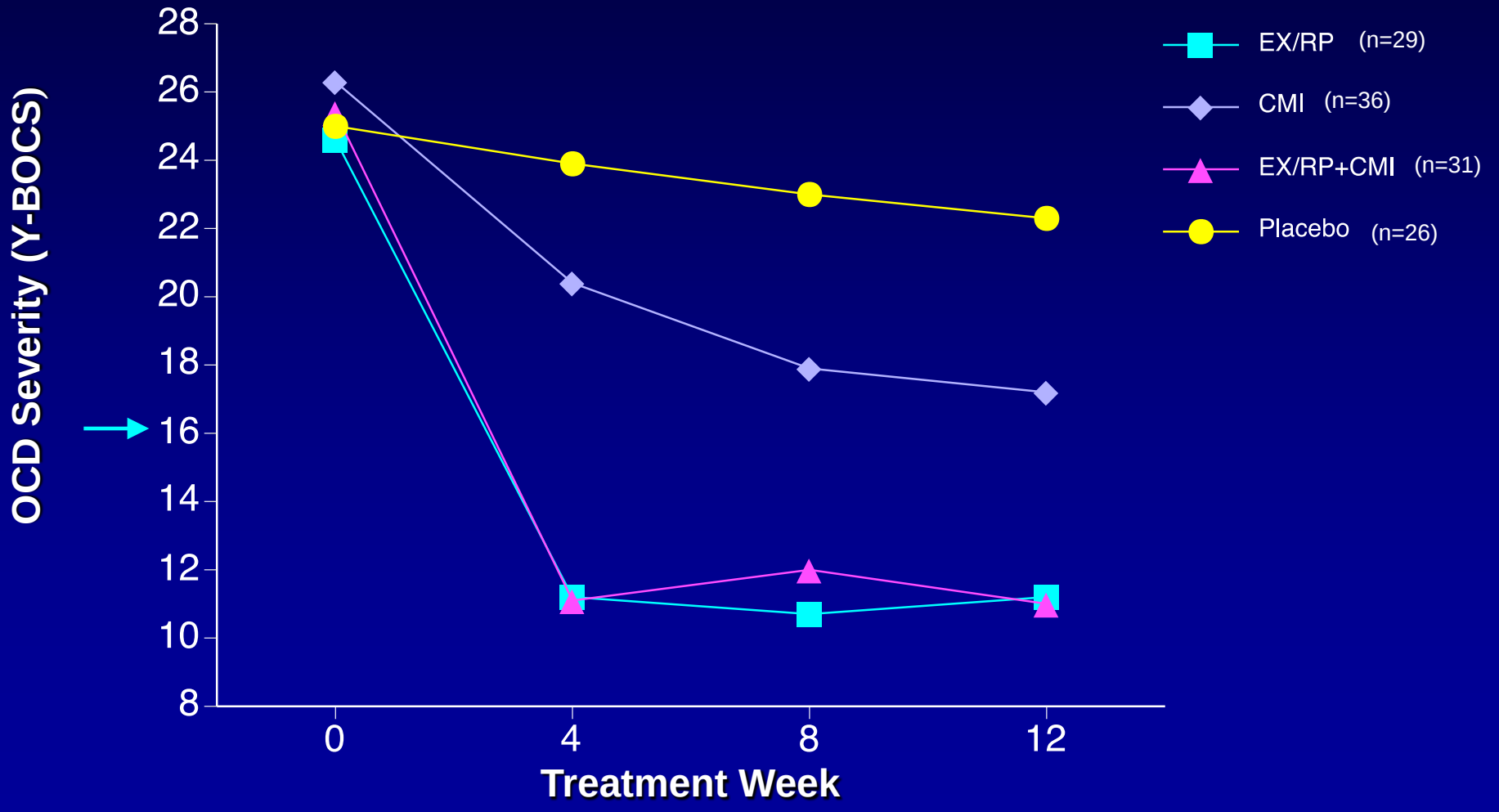
- Serotonin reuptake inhibitors (SRIs)
  - clomipramine
  - Selective SRIs: fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram,* escitalopram* *(*not FDA approved for OCD)*

- Cognitive-Behavioral Therapy
  - Exposure and Response/Ritual Prevention (EX/RP or "exposure therapy" or ERP)

How effective are SRIs versus EX/RP?

Comparing EX/RP, CMI, and EX/RP+CMI

EX/RP or EX/RP+SRI > SRI > PBO



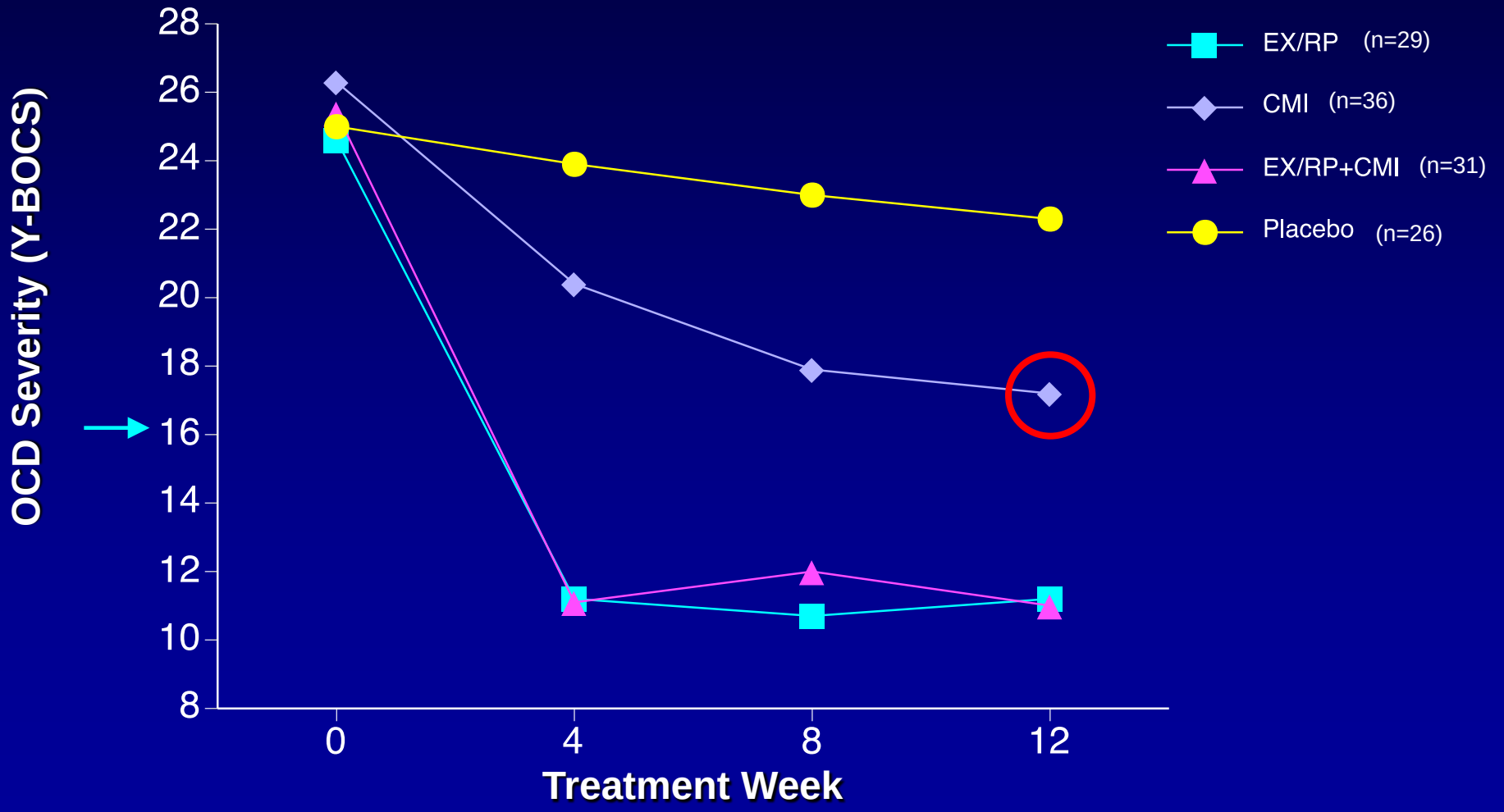
Foa et al. (2005) Am J Psychiatry

Conclusions

- EX/RP and SRIs are both efficacious for OCD
- EX/RP can be superior to SRIs
  - *when delivered intensively by skilled therapists to patients without significant depression*
- EX/RP+SRI was not clearly superior to EX/RP alone
  - *when treatments are started together and EX/RP is delivered optimally*

Comparing EX/RP, CMI, and EX/RP+CMI

EX/RP or EX/RP+SRI > SRI > PBO



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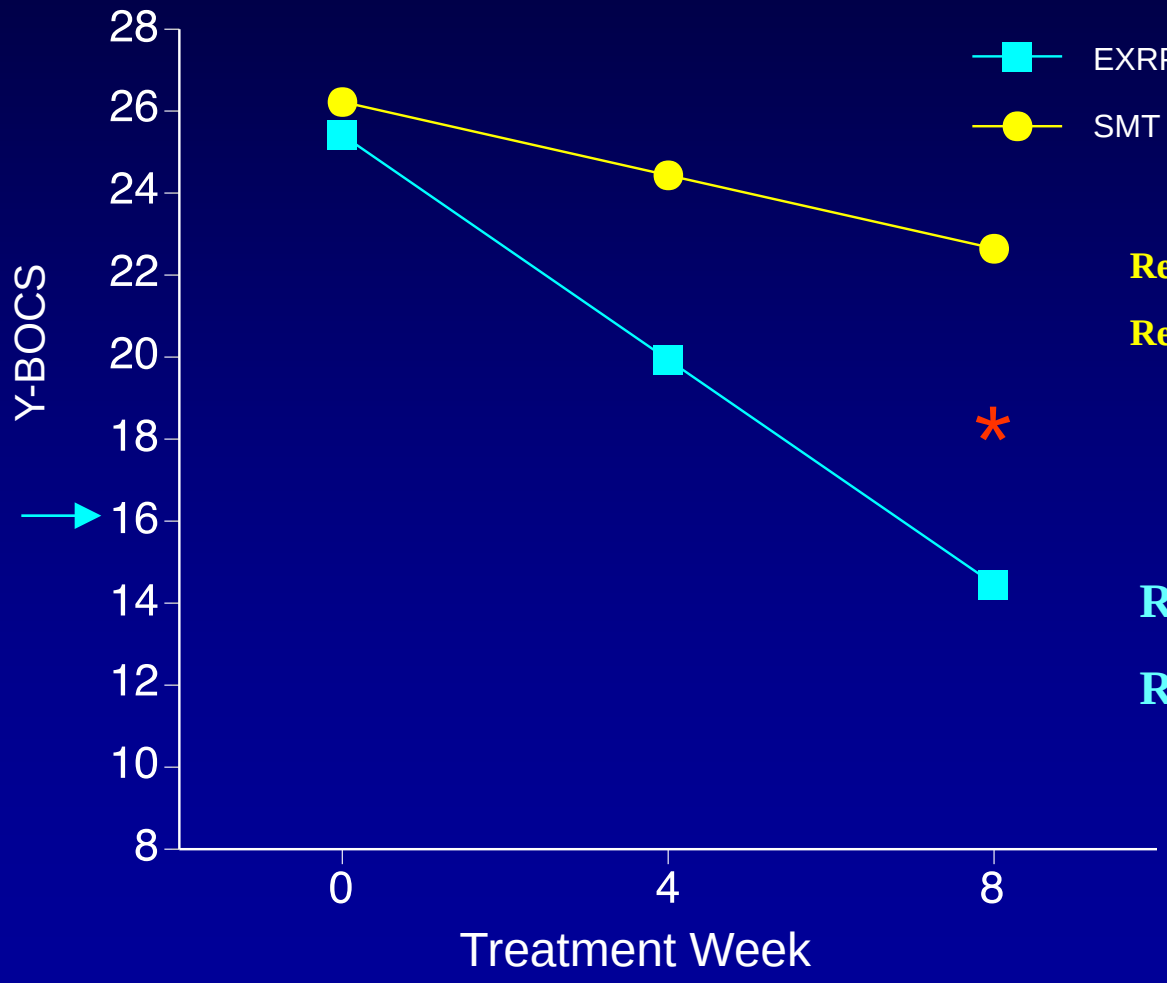
Can EX/RP augment SRI effects?

Augmenting SRIs with CBT

EX/RP > Stress Management Therapy



Response: 18/54 (33%)

Remission: 2/54 (4%)

Response: 40/54 (74%)

Remission: 18/54 (33%)

Simpson et al. (2008) Am J Psychiatry

Conclusions

- EX/RP can augment SRIs when delivered sequentially.
  - *responders are likely to maintain gains at 6 months (Foa et al. 2013)*

- After SRI+EX/RP, some (*not all*) achieve remission.

How does EX/RP compare to antipsychotic augmentation?

Unpublished data

(Simpson, Foa et al., accepted for publication in JAMA-Psychiatry)

Conclusions

- OCD patients on SRIs with ongoing symptoms should be offered EX/RP prior to antipsychotics.
  - *Whether OCD patients on SRIs who fail EX/RP can benefit from antipsychotics remains unknown.*

- Alternative medication strategies are needed.

Summary

- SRIs and EX/RP are each effective treatments for OCD
  - SRIs: 40-60% respond but ≤ 25% will achieve minimal symptoms
    - Limitations: *partial effects, SRI side effects*
  - EX/RP: 60-80% respond and ~50% achieve minimal symptoms
    - Limitations: *access, adherence, relapse*

- OCD patients on SRIs with symptoms should be offered EX/RP.
  - After SRI+EX/RP, some (~40%) will achieve remission!

******New study funded by NIMH being conducted in NYC and Philadelphia!***

- For nonresponders to SRIs+EX/RP, new treatments are needed.

What causes OCD?

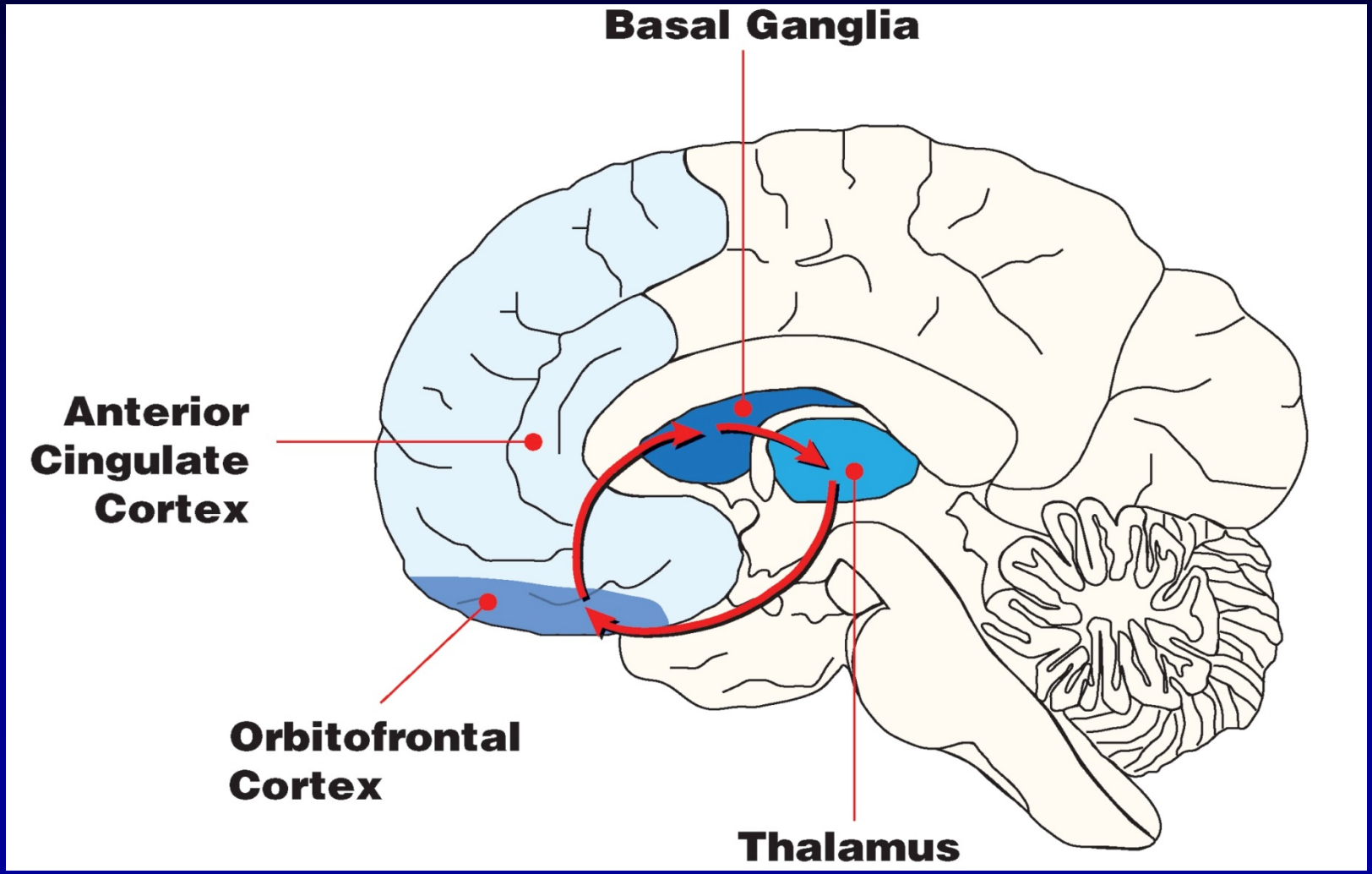
What Causes OCD?

- Pathophysiology (*How does the brain produce O+C?)*
  - Working model: Obsessions and compulsions are caused by specific brain circuits that are not functioning properly.

- Etiology (*How did the brain develop this problem?)*
  - Genes
  - Metabolic causes
  - Infectious agents and autoimmune mechanisms
  - Neurological insults
  - Environmental causes

GENES X ENVIRONMENT X DEVELOPMENT

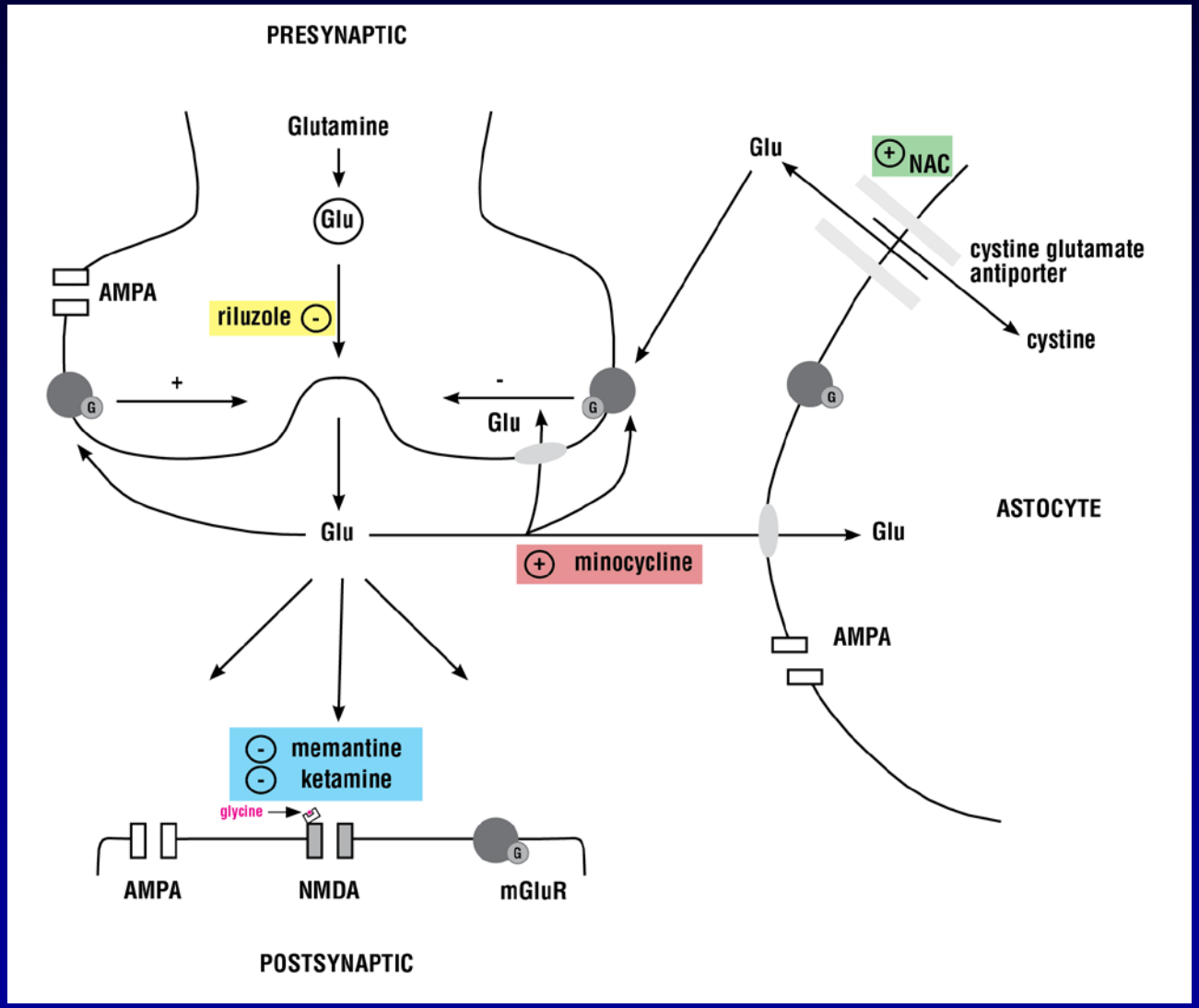
OCD: A Hyperactive Brain Circuit



Unpublished data

(Ahmari et al., accepted for publication in Science)

New developments: Glutamate modulators



Unpublished data

(Rodriguez et al, under review)

Opportunities and Challenges

Current studies for people with OCD

- Clinical research: ***for patients of today***
  - Examining how best to combine pharmacotherapy and psychotherapy
    - ***Can OCD patients on SRIs who are well after EX/RP safely discontinue their SRI?***
  - Testing novel treatment strategies
    - ***Glutamate modulators (e.g., minocycline, ketamine)*** **BBRF/NARSAD**
    - ***Transcranial Magnetic Stimulation***

- Neurobiological research: ***for patients of tomorrow***
  - Studying brain circuits implicated in OCD **BBRF/NARSAD**
  - Identifying shared & distinct brain correlates of behavior across disorders
  - Examining brain mechanisms using animal models **BBRF/NARSAD**

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