Transforming Treatment Outcomes for People with OCD

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NewYork-Presbyterian

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    - Janssen provided risperidone at no cost for NIMH-funded study (2006-2012)
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Why Do Biomedical Research?

To transform how we diagnose and treat illness and to pave the way to early intervention & cures

Why Do Biomedical Research?

but there is a gap…

Bridging the Gap with Patient-Oriented Research

Identifying Mechanisms & Targets for Intervention



Translating from Basic Science


GOAL
To pave the way to early intervention & cures

Testing & Improving Treatments



Disseminating & Implementing

BASIC SCIENCE

CLINICAL PRACTICE

What is OCD
and
how do we treat it *today*?

Hallmarks of OCD

- Core Features:
  - Obsessions: repetitive thoughts, images, or urges (*intrusive, distressing*)
  - Compulsions: repetitive behaviors or mental acts
  - Symptoms are distressing, time-consuming, and impairing

- Associated Features:
  - Range of content and fears *(“symptom dimensions”)*
    - *contamination, harm, symmetry/exactness, taboo thoughts*
  - Different affects (*anxiety & panic, “not just right,” disgust*)
  - Varying insight (*good to absent*)
  - Various comorbidity (*e.g., anxiety, depressive, tic, or eating disorders)*

Diagnostic and Statistical Manual of Mental Disorders (DSM-5), 2013;
International Classification of Diseases (ICD-11), 2022

OCD is 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

First-line Treatments for OCD that Work

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

- Cognitive-Behavioral Therapy (CBT)
  - Exposure and Response/Ritual Prevention

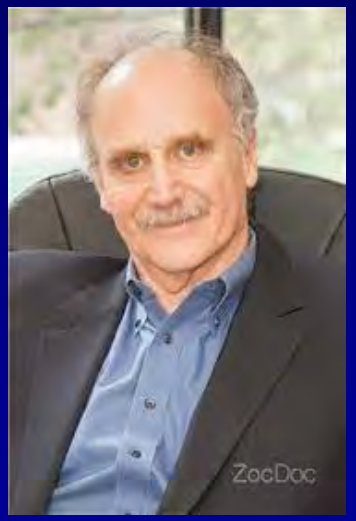
    (*EX/RP*, *exposure therapy*, *E/RP*)

What is CBT Consisting of EX/RP?

- Key Procedures:
  - Exposures (*in vivo [aka live]* and imaginal)
  - Ritual prevention
- Goals:
  - To disconfirm fears & challenge distorted beliefs
  - To break the habit of ritualizing & avoiding
  - *To improve functioning and quality of life!*
- Standard Format:
  - 2 planning sessions plus 15 exposure sessions (*2x/week or more*)
  - Daily homework and home visits to promote generalization

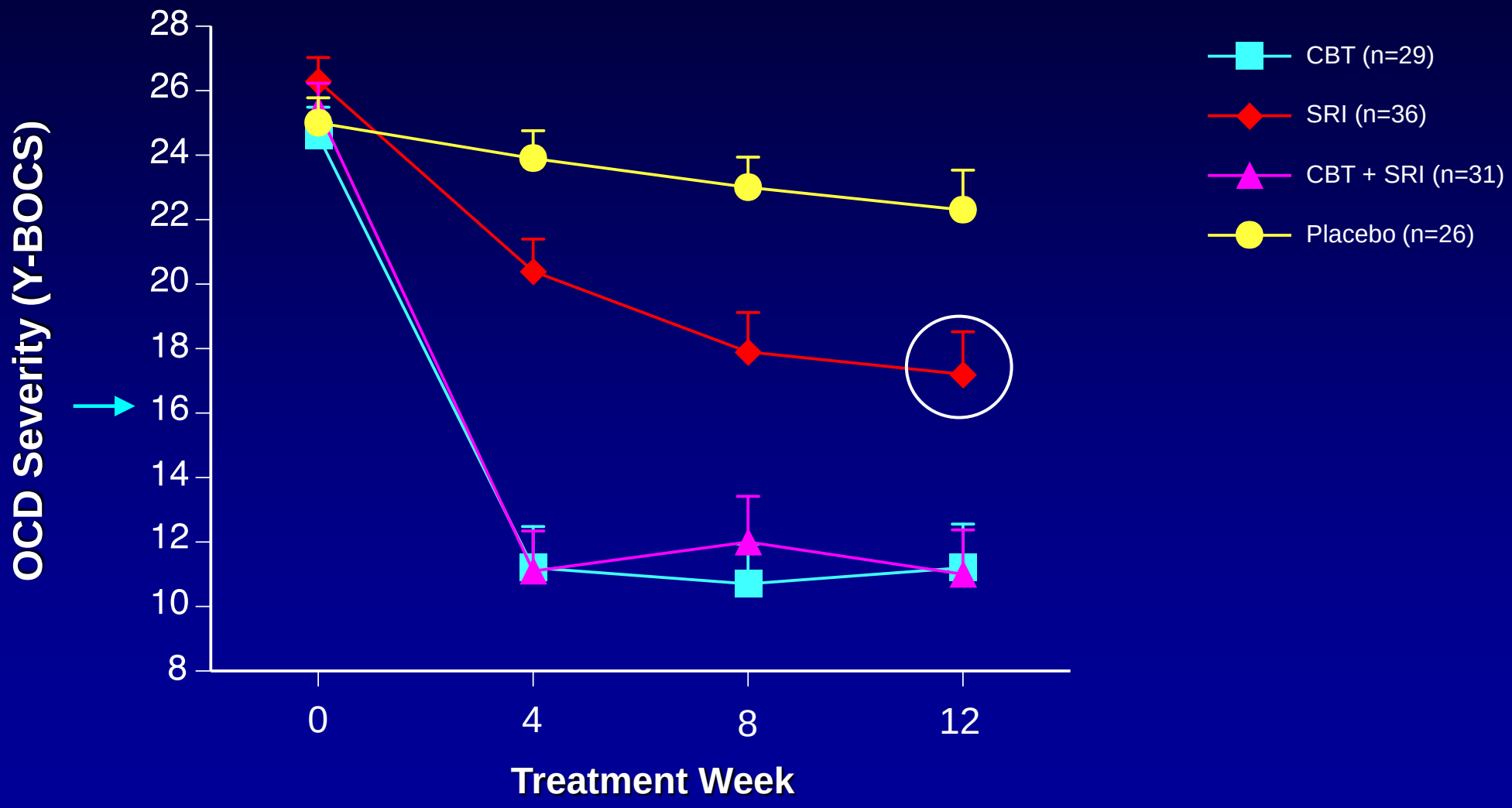
Kozak & Foa (1997); Foa et al. (2012)

What is the best treatment for OCD: *an SRI, CBT, or their combination*?



Funding: NIMH R01-045404 (PI: Foa); NIMH R01-045436 (PI: Liebowitz)

What is the Best Treatment for Adults with OCD?



Foa, Liebowitz et al. (2005) Am J Psychiatry

For OCD Patients on SRIs with Symptoms

Next Question: Is adding EX/RP to SRIs better than:

1) a psychosocial control?

Funding: NIMH R01-045404 (PI: Foa); NIMH R01-045436 (PIs: Liebowitz & Simpson)

2) an antipsychotic medication?

Funding: NIMH R01-045436 (PI: Simpson); NIMH R01-045404 (PI: Foa)

Simpson, Foa et al. (2008) Am J Psychiatry; Foa, Simpson et al. (2013) J Clin Psychiatry; Simpson, Foa et al. (2013) JAMA-Psychiatry; Foa, Simpson et al. (2015)

Take Home Messages from a series of trials:

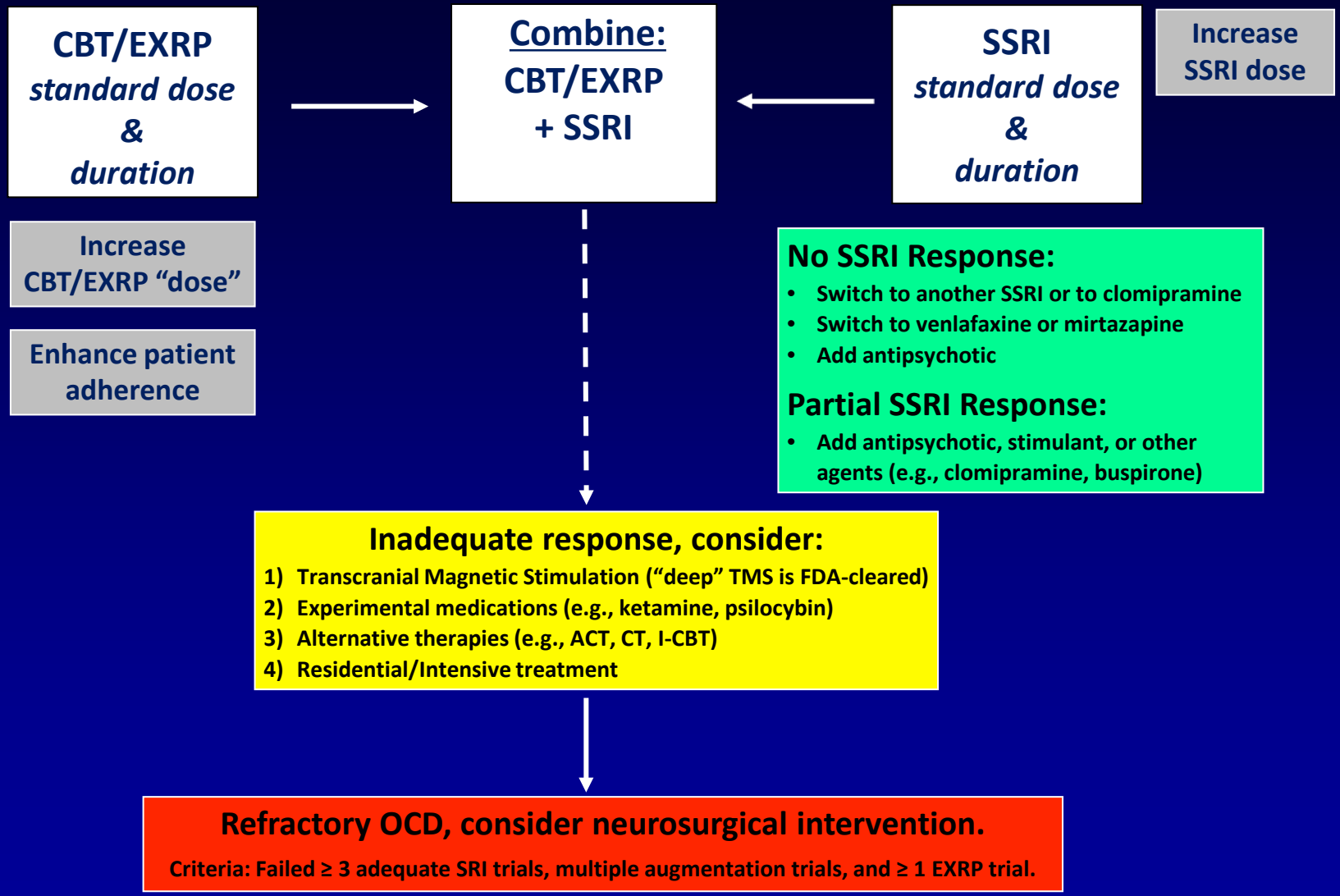
- SRIs: Effective for some, but response is usually partial.

- EX/RP: Effective for more, but patient adherence is key.
  - *Simpson et al. (JCCP, 2011):* Predicts acute outcome
  - *Simpson et al. (J Clin Psychiatry, 2012):* Predicts 6-month outcome
  - *Wheaton et al. (BRAT 2016):* Early adherence forecasts outcome

- SRIs + EX/RP: ~40% attain minimal symptoms with 17 sessions
  - Q1: Who attains minimal symptoms? *Simpson, Foa et al. (2021) BRAT*
  - Q2: Can they then stop their SRI? *Foa, Simpson et al. (2022) JAMA-Psychiatry*

Funding: NIMH R01-045404 (PI: Foa); NIMH R01-045436 (PI: Simpson)

OCD Treatment Algorithm for Adults



American Psychiatric Association's Practice Guidelines for OCD (2007, 2013);
National Institute for Health and Care Excellence (www.nice.org.uk); OCD Treatment Guide (www.iocdf.org)

Challenge #1:

Most with OCD do not receive evidence-based treatment.

IMPACT-OCD: Improving Assessment, Care, & Treatment

- Goal: To increase awareness about OCD and build capacity of community clinicians across New York State to diagnose and treat individuals with OCD.

- Partners:

Center for OCD and Related Disorders

Center for Practice Innovation (CPI)

NYS-OMH

IMPACT-OCD Team NOW!






CENTER FOR OCD & RELATED DISORDERS AT COLUMBIA PSYCHIATRY





Center for Practice Innovations℠
at Columbia Psychiatry
New York State Psychiatric Institute
Building best practices with you.






NEW YORK STATE OF OPPORTUNITY. | Office of Mental Health

IMPACT OCD

IMPROVING PROVIDERS' ASSESSMENT, CARE DELIVERY AND TREATMENT OF OCD

IMPACT-OCD: Phases of Development

Phase 1:
June 2018 – May 2020

- **Workforce Development**

Phase 2:
June 2020 – October 2023

- **Workforce Development**
- **Early detection**

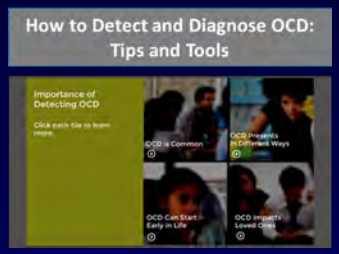
Phase 3:
2023+

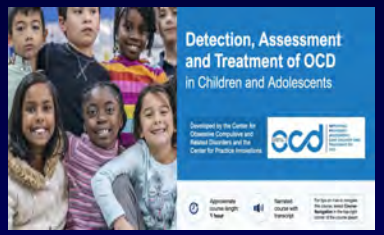
- **Workforce Development**
- **Early detection**
- **Build capacity to treat**

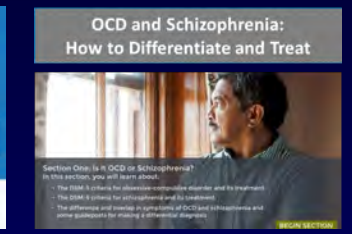
IMPACT OCD
IMPROVING PROVIDERS' ASSESSMENT, CARE DELIVERY AND TREATMENT OF OCD

Phase 1: Workforce Development

E-training Modules







Online Toolkits

https://practiceinnovations.org/initiatives/impact-ocd/resources/toolkits

- Resources for providers
- Resources for individuals and families

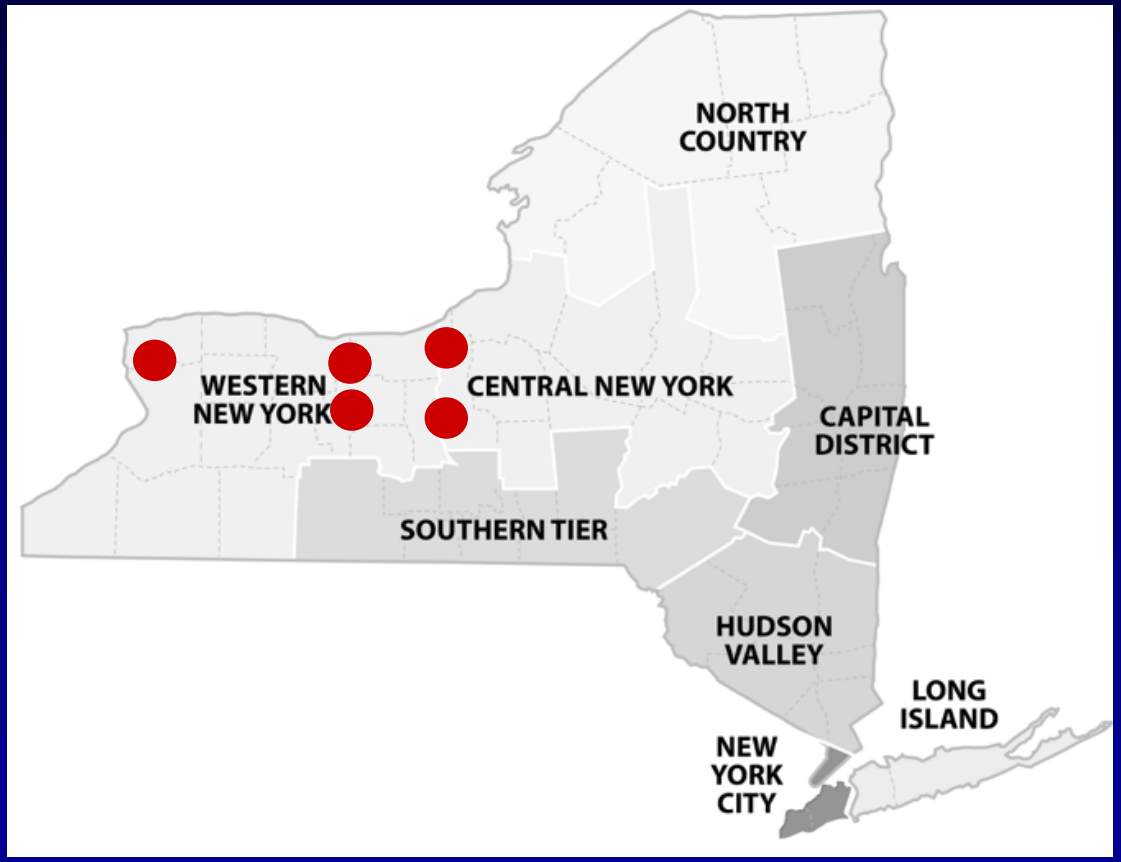
Expert Consultations

- Assessment
- Psychotherapy
- Medication

Phase 2: Early Detection-Pilot Screening Project

Partnership with Certified Community Behavioral Health Clinics

- Develop & implement OCD screening tool
- Online support from IMPACT-OCD clinicians
- Help with referrals



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IMPACT OCD
IMPROVING PROVIDERS' ASSESSMENT, CARE DELIVERY AND TREATMENT OF OCD

Ultimate Goal

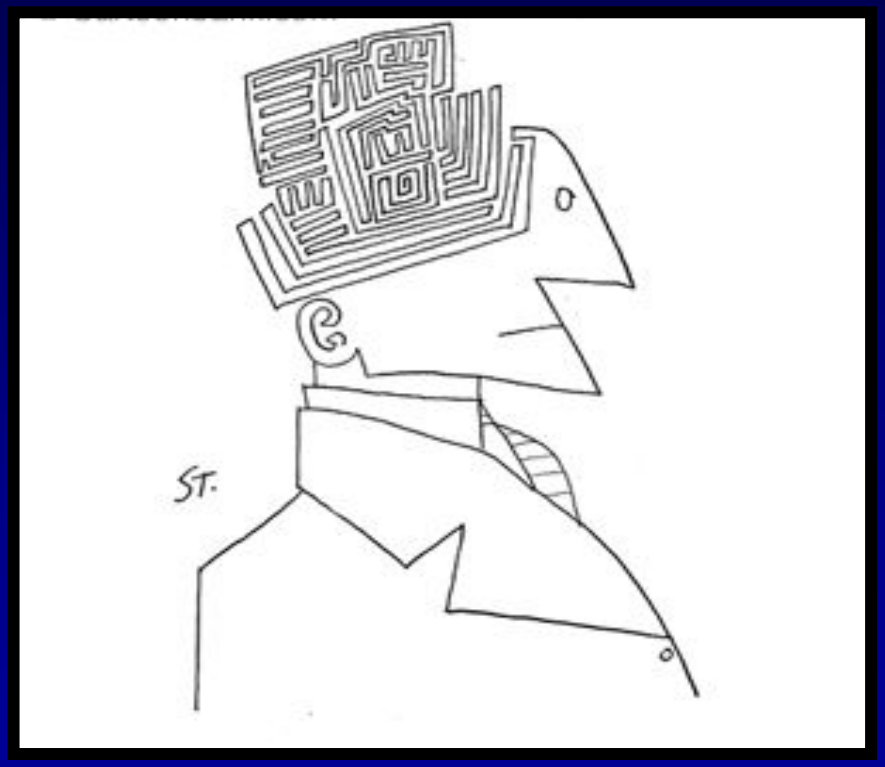
Early Detection

Access to Treatment

Early intervention for OCD

Challenge #2:

Current treatments work only for some.



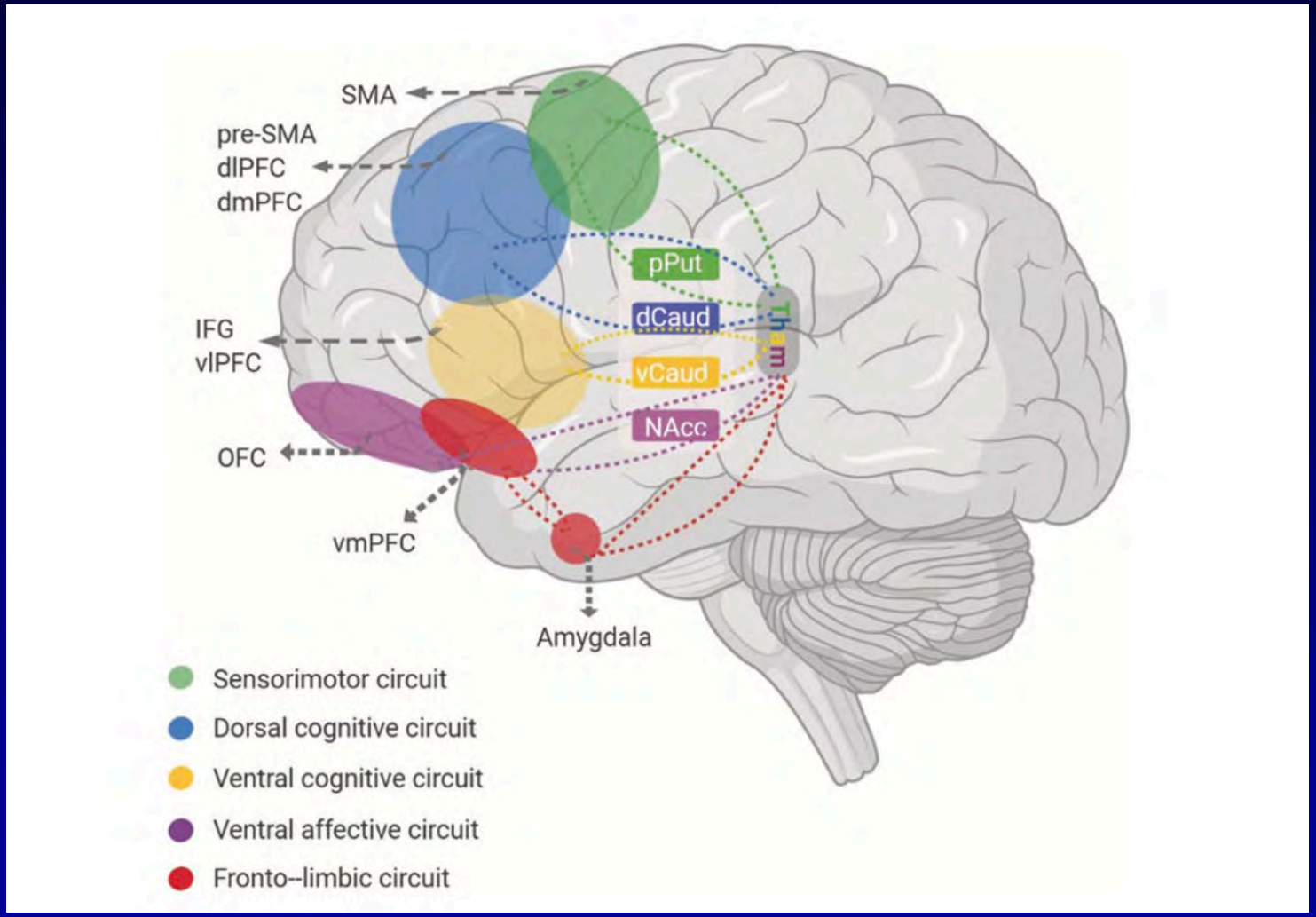
Saul Steinberg, The New Yorker

What Causes OCD?

- Pathophysiology (*How the brain produces O+C.)*
  - Working model: Specific brain circuits are not functioning properly.
  - Neurocognitive and neurobehavioral alterations *include*:
    - threat processing/fear extinction
    - balance between goal-directed and habitual behavior
    - cognitive control/response inhibition
    - reward processing

- Etiology (*How the brain developed dysfunction.)*
  - genes (*family studies, twin studies, candidate gene, linkage, GWAS….*)
  - infectious agents and autoimmune mechanisms (*PANDAS/PANS/CANS)*
  - neurological insults
  - metabolic causes
  - environmental causes

Multiple Brain Circuits Implicated in OCD



Shephard et al. (2021)

Challenges Interpretating Brain Imaging Data

- What is cause versus effect?
- Do all OCD patients have the same brain dysfunction?
- Are neuroimaging findings robust and reproducible?

Global Initiative: To Identify Robust Biosignatures

Aim #1: To identify brain signatures of OCD

Aim #2: To link these to different clinical profiles of OCD

NIMH R01-113250 (PIs: Simpson& Wall, Miguel&Shavitt, Reddy, Stein& Lochner, van den Heuvel)

Study Design

- Sample:
  - N=250 unmedicated adults with OCD
  - N=100 unaffected siblings
  - N=250 healthy volunteers
    - Match: age, sex, educational level/IQ

- Measures:

Clinical Symptoms

- OCD: severity, dimensions, age of onset, insight
- Depressive severity
- Anxiety severity
- Treatment history
- Other related symptoms

*Neurocognitive Tasks**

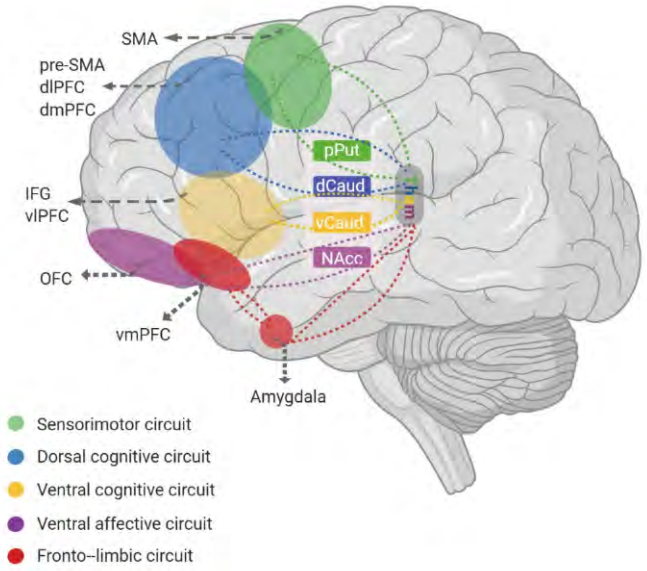
- Updating and Planning
- Response inhibition
- Temporal Discounting
- Emotional Stroop
- Reinforcement learning

**tapping same brain circuits*

Neuroimaging

- Structure (T1)
- Resting activity (rs-fMRI)
- White matter tracts (DTI)
- Multimodal fusion

Toward Precision Psychiatry



1

Fronto-limbic circuit

Clinical profiles:
Dysregulated fear
Intolerance of uncertainty

Treatment approach:
Reduce fronto-limbic hyperactivity
Increase dorsal cognitive top-down control

Potential treatment methods:
CBT / SSRIs
Amygdala/vmPFC fMRI-neurofeedback
dlPFC rTMS
ALIC deep brain stimulation

2

Sensorimotor circuit

Clinical profiles:
Sensory phenomena
Excessive habit-formation

Treatment approach
Reduce sensorimotor circuit overactivity
Regulate insula activity (sensory phenomena only)

Potential treatment methods:
Habit-reversal training
SMA rTMS
H-coil insula rTMS
Ondansetron

3

Ventral cognitive circuit

Clinical profiles:
Impaired response inhibition

Treatment approach:
Increase ventral cognitive circuit hypoactivity

Potential treatment methods:
IFG fMRI-neurofeedback
STN/VS deep brain stimulation

4

Ventral affective circuit

Clinical profiles:
Altered reward responsiveness

Treatment approach:
Restore reward mechanisms

Potential treatment methods:
SSRIs
Dopamine-acting medication (e.g. methylphenidate)
NAcc fMRI-neurofeedback
NAcc deep brain stimulation

5

Dorsal cognitive circuit

Clinical profiles:
Executive dysfunction

Treatment approach:
Increase hypoactive dorsal cognitive circuit function

Potential treatment methods:
CBT
Methylphenidate
dlPFC and pre-SMA rTMS/tDCS

Shephard et al. Molecular Psychiatry (2021)

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CLINICAL PRACTICE

Collaboration & Support!

- Collaborators
  - Clinical Trials: Edna Foa and team at UPENN
  - IMPACT-OCD: Sapana Patel and team at the Center for Practice Innovations & Bob Myers and Sarah Kuriakose and the team at the New York State-Office of Mental Health
  - The OCD Global Team: Brazil (Miguel, Shavit); India (Reddy); Netherlands (van den Heuvel); South Africa (Stein, Lochner); USA (Simpson, Wall)

- Financial support
  - National Institutes of Mental Health (NIMH)
  - New York State Office of Mental Health
  - Private Foundations (Brain and Behavior Foundation, International OC Foundation)
  - Philanthropy

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Current Members:
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