Rapid-Acting Treatments for OCD

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NIMH (PI: Rodriguez)
- K23 Novel Interventions for Adults with OCD
- R01 NMDAR Modulation As A Therapeutic Target and Probe of Neural Dysfunction in OCD

Foundations/Donors (PI: Rodriguez)
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Other (PI: Rodriguez)
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Industry (Consultant: Rodriguez)
- Allergan
- Rugen Therapeutics
- BlackThorn Therapeutics
- Naurex (donated study drug at no cost for rapstinel study)
OCD: A Chronic, Disabling Disorder

Mother and Child, from The London Studio

Koran et al., 2007; Koran and Simpson, 2013
OCD: Hyperactive Fronto-Striatal Brain Circuits

Rosenberg et al., 2000; Pittenger et al., 2011; Maia et al., 2008; Ahmari et al., 2013; Burguiere et al., 2013; Wood and Ahmari, 2015
Ketamine
Ketamine Decreases OCD

Ketamine: NMDA glutamate receptor antagonist

Individuals with OCD (n=15) randomized to IV ketamine or saline

Rodriguez et al., *Neuropsychopharmacology*, 2013
Study Design (Flow)

31 Individuals Assessed for Eligibility

16 Excluded for not meeting entrance criteria
- 4 OCD was not the primary diagnosis
- 3 were not 18-55 years old
- 2 had subclinical OCD (YBOCS <16)
- 2 comorbid bipolar disorder
- 2 had severe depression (HDRS >25)
- 2 had an unstable medical condition
- 1 had obsessions < 8 hrs a day

15 Enrolled/Randomized

Arm A
- 8 Ketamine
- At least 1 week apart
- Mean 2.1 weeks (SD 13 days)
- 8 Placebo

Arm B
- 7 Placebo
- 7 Ketamine

Rodriguez et al., Neuropsychopharmacology, 2013
First Phase Only

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8 Ketamine

At least 1 week apart
Mean 2.1 weeks (SD 13 days)

Arm B
7 Placebo

8 Placebo

7 Ketamine

Rodriguez et al., Neuropsychopharmacology, 2013
Ketamine Rapidly Reduces OCD

Rodriguez et al., *Neuropsychopharmacology*, 2013
First Phase

Proportion Responders 1 week post infusion
(35% reduction in YBOCS Score)

Ketamine (N=8)       Saline (N=7)

* p < 0.05

Rodriguez et al., Neuropsychopharmacology, 2013
## Side Effects

<table>
<thead>
<tr>
<th>Side effects in order of frequency</th>
<th>TOTAL N=15 (8 Ketamine, 7 Saline)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Feelings of unreality/ Dissociation</td>
<td>8</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
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</tbody>
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Mild transient changes in blood pressure and heart rate observed on infusion day consistent with MDD studies that show mean change pre/post IV ketamine of less than 20 mm Hg systolic and 10 mm Hg diastolic.

Rodriguez et al., Neuropsychopharmacology, 2013
Murrough, et al., 2013
Quotes from Responders after Ketamine

Responders (4 out of 8):

1. “I feel as if the weight of OCD has been lifted…I want to feel this way forever”

2. “I feel like someone is giving me an explanation [for my OCD]”

3. “I don’t have any intrusive thoughts. I was laughing when you couldn’t find the key, which normally is a trigger for me. This is amazing, unbelievable. This is right out of a movie.”

4. “I tried to have OCD thoughts, but I couldn’t”
Summary

First study showing ketamine can decrease intrusive thoughts in the absence of SRIs

Glutamate modulation may be a rapid-acting therapeutic target for OCD

Rodriguez et al., *Neuropsychopharmacology*, 2013
Future Directions

Mechanism of Ketamine’s Effect (NIMH R01)

Who gets better? Why?
What we need:

Research Partners (Study Participants)
ocdresearch@stanford.edu

Research Collaborators and Funding
Translate discoveries into new rapid treatments
Impact

Demonstrate Rapidly Acting Tx Possible

Shed light on severity of OCD

Decrease Stigma

1 Million Steps 4 OCD Walk     Oakland, CA, June 4, 2016
Sacramento, CA, June 10, 2017

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