The Impossible Dream: Treatment Approaches for the Most Challenging Suicidal Adolescents

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Overview of Talk -

- Description of our Integrated Treatment Approach
- Results from First RCT
- Results of RCT nearing completion
- **SPOILER ALERT!**
- Why failure to replicate? An exercise in hindsight bias
- What do we do with the most treatment resistant of treatment resistant patients?
Integrated Treatment for Depression, Suicidality, and Alcohol Abuse
(Esposito-Smythers, Spirito, et al, 2011)

- From CWD-A to TADS to TORDIA to TRYADS
- Manualized modular treatment – suitable to address multiple presenting problems. Our addition – to address substance use
- CBT techniques used to remediate maladaptive cognitions and behaviors that underlie alcohol/drug abuse and suicidality
- Weekly monitoring of suicidality and substance use to help prevent relapse
Treatment Protocol Schedule

- Three treatment phases
  - Active: 6 months of weekly sessions, if necessary
  - Maintenance: 3 months of bi-monthly sessions
  - Booster: 3 months of monthly sessions
- Two therapists assigned to each case
  - Adolescent therapist
  - Parent/family therapist
Treatment protocol

- Why so intensive?
- Why two therapists?
Integrated Treatment Protocol: Core Sessions

- Rapport Building / Goal Setting / Safety Planning
- Problem-solving
- Cognitive restructuring
- Affect regulation / Distress Tolerance
- Behavioral Activation / Increasing Healthy Pleasant Events
Integrated Treatment Protocol: Alcohol/Drug Sessions

- Motivational Interview
- Enhancing Social Support Networks
- Alcohol/Drug Refusal Skills
- Coping with Cravings
- Planning for Emergencies that may trigger suicidality or drug use
Integrated Treatment Protocol: Optional Sessions

- Distress Tolerance
- Chain Analysis
- Assertiveness Training
- Anxiety Exposure
Integrated Treatment Protocol: Family Sessions

- Family Communication
- Family Problem-Solving
- Increasing Positive Family Interactions
Integrated Treatment Protocol: Parent Training Sessions

- Parental Monitoring
- Parenting Beliefs
- Parent Affect Regulation
- Parent Problem-Solving
- Attending to Child and Self
- Contingency Management
TRYADS Study Participants

- 36 adolescents (19 in EXP and 17 in E-TAU); 12 M, 24 F
- 72% on medication at study entry
- Prior therapists: 0-5, mean = 2
- Depressed for an average of 2.8 years
- Average of a 2.9 year treatment history
- Suicidality: 100% suicidal ideation; 75% suicide attempt
Other Psychiatric Outcomes 18M

**Percentage Requiring ER Services**

- EXP: 16%, n = 3
- E-TAU: 59%, n = 10

\[ X^2(1) = 7.20, \, p < 0.01 \]
\[ d = .93, \text{large effect} \]

**Percentage Requiring Inpatient Services**

- EXP: 16%, n = 9
- E-TAU: 53%, n = 10

\[ X^2(1) = 5.57, \, p < 0.05 \]
\[ d = .81, \text{large effect} \]
Other outcomes

- EXP had fewer conduct related problems (e.g., arrests, suspensions, running away)
- Greater decline in suicidal ideation in EXP
- Greater declines in alcohol and cannabis use in EXP
InVest – Current RCT

- Adapted protocol slightly to:
  - Enhance transdiagnostic applications
  - Focused more on a set of core skills that could be used with parent, teen, family to enhance skill acquisition and generalizability
  - Added Parent Emotion Coaching and Validation Skills
InVest – Current RCT

- Two group randomized controlled trial - Integrated CBT versus Enhanced Treatment-as-Usual (E-TAU)
- More than one risk factor – NSSI, prior suicide attempt, and/or substance abuse
- All recruited from inpatient psych unit
Suicide Ideation Questionnaire (SIQ) Cut-off 30
- \( M = 51.8, \ SD = 21.0 \)
- Number of days in the past 30 with SI \( M = 17.8, \ SD = 11.3 \)

Columbia Suicide Severity Rating Scale (C-SSRS)
- 66% lifetime SA (Mean age at 1\textsuperscript{st} attempt = 13.4 years, SD = 2.1 years)
- 19% lifetime interrupted attempts
- 34% lifetime aborted attempts

Children’s Depression Rating Scale
- Cut off 64; \( M = 73.0, \ SD = 6.7 \)
Sample Descriptives

- **K-SADS diagnoses**
  - MDD $\rightarrow$ 88% (remainder had depression NOS)
  - 68% had at least 1 suicide attempt in social network
- **Concurrent diagnoses**
  - GAD 40%
  - ODD/CD 24%
  - PTSD 24%
  - SUD 26%

- **NSSI**
  - Lifetime 87%
  - Past 30 days 70%
### 18 month cumulative outcomes – Based on DSMB data; 2/3 of follow-up data

<table>
<thead>
<tr>
<th></th>
<th>EXP</th>
<th>E-TAU</th>
<th>LONG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attempts</td>
<td>29%</td>
<td>22%</td>
<td>37%</td>
</tr>
<tr>
<td>Psych Hosp/SA</td>
<td>19%</td>
<td>16%</td>
<td>27%</td>
</tr>
<tr>
<td>Psych Hosp/Total</td>
<td>24%</td>
<td>33%</td>
<td>51%</td>
</tr>
</tbody>
</table>

| N                | 52  | 55   | 49   |
A failure to replicate: At least we are in good company!

PsychFileDrawer, dedicated to replication of published articles in experimental psychology:

**Replication rate 3 out of 9** (33%)

Bayer scientists examined 67 target-validation projects in oncology, women's health, and cardiovascular medicine:

**14 out of 67 projects** (about 21%).

Amgen reproduce the findings of 53 “landmark” articles in cancer research:

**6 out of 53 studies** (about 10%).
What might account for our failure to replicate? Treatment Protocol Differences

- Modules used in the treatment protocol? Less use of substance use modules
- Parent management of alcohol misuse behavior is more straightforward than management of self-injury
- Many parents ambivalent about teens smoking marijuana
- Parental management of NSSI much trickier
Treatment Protocol differences

- Fidelity and Competency rating comparable across trials
- More contact with therapists due to the explosion of texting between trials? Is too much contact iatrogenic?
- Therapist burnout? Much larger study and more patients seen by each therapist
What might account for our failure to replicate?

Was treatment as usual (TAU) of high quality?
Did TAU improve since last trial?
What is the right amount of treatment for chronically suicidal youth?

- E-TAU attended less treatment
- Does stirring up issues result in more acute distress but long term gain?
- Is an intensive treatment protocol iatrogenic when residential treatment is really what is indicated?
- Is conducting therapy at the psychiatric hospital contraindicated? And do parents use hospitalization for a respite?

“I fear for my life”
Why was there a failure to replicate?

II. SAMPLING FACTORS –

Most impaired sample of the 3 trials we have conducted on this unit

Subject 001

“They’re never going to take me alive”
Why was there a failure to replicate?

II. SAMPLING FACTORS -

A. Small sample size in original study

B. It was the same recruitment source, but clinical characteristics differed some:
   SUD in only 26% - Did they do better?

C. Is inpatient treatment iatrogenic?
   Our treatment team only initiated 5 of 18 readmissions
Sampling Factors: Cohort difference?

NSSI

- Lifetime 87%
- Past 30 days 70%
- NSSI/suicide attempts habituate individuals to the experience of engaging in dangerous self-injurious behavior (Joiner, 2005)
- Suicidal behavior makes the suicidal cognitive schema more easily accessible in future stressful situations (Beck et al, 1996)
Cohort differences? Social Media and NSSI

Social media often a driving force in perpetuating NSSI and suicidal behavior

Changing an adolescent’s social media presentation may be a cognitive intervention strategy
II. Sampling Factors: Gender and Sexual Identity issues

- About 40% identified as Lesbian/Gay – a primary issue in about half of these patients
- No one identified as transgender in the original RCT
- 3 participants in current study in experimental arm – 2 had multiple hospitalizations
- Identifying as transgender may have caused more immediate distress even if helpful in the long term
Sampling factors: “Rule of Thirds”

- Schizophrenia research (Stephens, 1978):
  - One-third of treated patients recover completely, one third improve,
  - And one-third remain impaired or deteriorate.
- Is there a tipping point past which the amount of variance accounted for by treatment is negated by level of patient symptomatology?
- Moderator analyses
Assessment differences biased in favor of E-TAU?

Suicidal behavior

Experimental protocol desensitized patients to reporting suicide attempts relative to standard care, especially with respect to fear of hospitalization.

Severity of attempts was much higher in TAU than the experimental protocol

5 attempts were found in medical record review in the E-TAU condition versus 0 in experimental
How do we improve care for the 30%?

In our experimental designs?

- Trial terminated at 12 months and then had to find new therapists

- **Experimental patients do worse in the period between 12 and 18 month follow-up:**
  - 5 attempts versus 1 attempt
  - 6 versus 3 psych hospitalizations

Chronic care model?
Is there any treatment pattern that would inform future treatment?

- After 1 session - 13%
- Between 2 and 6 - 29%
- Between 7 and 10 - 21%
- Between 13 and 20 - 21%
- Between 25 and 43 - 16%

High risk period lasts beyond the 1 to 3 month period after discharge.
The 30%: Is it their brains?
rTMS? To change a circuit or enhance therapy?
fMRI Feedback?

Or something being worked on in a start-up in Cambridge or Silicon Valley?
Cognitive Control Training (CCT):

- Computer-based sustained attention and working memory tasks
- Developed to explicitly target the DLPFC-amygdala circuit implicated in rumination and depression
- Theory: increase prefrontal (DLPFC) function to remediate the prefrontal deficits that lead to limbic dysregulation and rumination.

(Siegle et al, 2009)
We considered for one patient who ended up getting ECT
Neurotransmitter metabolism and depression (Pan et al, 2016)

- TREATMENT RESISTANT DEPRESSED TEENS
  - Conducted a series of biochemical tests with a single treatment resistant adolescent
  - A cerebrospinal fluid deficiency in biopterin, a protein involved in the synthesis of several neurotransmitters, was discovered
  - 33 adolescents and young adults with treatment-resistant depression and 16 controls were then tested.
  - Although the specific metabolites affected differed among patients, the researchers found that 64 percent of the patients had a deficiency in neurotransmitter metabolism, compared with none of the controls.
  - In almost all of these patients, treating the underlying deficiency improved their depression symptoms, and some patients even experienced complete remission.
Which is easier to treat? The brain or the environment?

- Harsh environment hypothesis (Grandin, Alloy, Abramson, 2007)
- May arise from being situated in an adverse environment where exposure to negative external stressors is more frequent
- How much variance in symptoms does neural circuitry account for in a harsh environment?
It's not the brain, or environment, stupid, it's the gut!

How these differences in our microbial world influence the development of brain and behavior will be one of the great frontiers of clinical neuroscience in the next decade. Insel, 2012
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I WANT AN EASY PLATEAU,
SOME PLACE TO LAY MY
HEAD