



Arthur Sommer Rotenberg Chair in Suicide Studies



NEUROBIOLOGY OF PAIN PROCESSING AND SUICIDE: A POTENTIAL MARKER FOR SUICIDE RISK

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WHAT DOYOU NEED...









"Committed suicide"

"Died by suicide"

"Victim of mental illness" "Experiencing mental illness"

"Unsuccessful suicide"

"Attempted suicide"

American Foundation for Suicide Prevention; American Psychological Association

WHAT IS SUICIDE?

- Not a feeling; behaviour
- Reaction to deep emotional pain
- Not about wanting to die
- Seeing no options out



PREVALENCE OF SUICIDE

Worldwide 800,000 deaths by suicide per year

25-30 attempts for every suicide death Some Indigenous communities

(250 per 100,000)

2nd leading cause of death in people 15 to 34

WHO Preventing Suicide, 2014; Canadian Mental Health Association, Statistics Canada, 2009

WHO IS AT RISK FOR SUICIDE ATTEMPT?



Young Age Female Gender Single Status Low Income Life Stressors Social Isolation Mood Disorder Substance Abuse Trauma History Hopelessness Psychache Impaired Memory and Attention



Brain Volume Brain Activity Impaired Brain Chemistry Inflammation Genetics

BRAIN AREAS AFFECTED IN DEPRESSION AND SUICIDE



Treadway & Zald,, 2011

NEUROTRANSMITTERS



SUICIDE AND SEROTONIN

Mood and aggression

 Less serotonin predicted more lethal suicide behavior and severity of ideation over 2 years



Oquendo et al., 2016 JAMA Psychiatry

FROM SUICIDAL IDEATION TO ATTEMPT: What leads to the transition?



Chen et al., 2014; Public Health Agency of Canada, 2016

ISSUES IN SUICIDE RESEARCH

No clear characterization of 20% who will attempt	Risk Assessment not enough: "low risk" often attempt	Ideation not an ideal marker of attempt
Need long-term population data to confirm suicide rates	Prediction challenges	Neurobiology can help identify markers of acute risk/tx targets

TRANSITION FROM IDEATION TO ATTEMPT: INTERPERSONAL THEORY OF SUICIDE



Joiner, 2005

PAIN PROCESSING AND SUICIDE ATTEMPT



Physical Pain Threshold

= The level of stimuli when one begins to feel the pain

Physical Pain Tolerance

= The maximum level of pain that one can tolerate

Physical Pain Intensity

= Subjective rating of pain at a given intensity level



= The ability to endure psychological pain

Orbach et al., 1996a; 1996b; 1997; Cáceda et al., 2017; Kim et al., 2019; DeVille et al., 2020; Meerwijk & Weiss, 2018; Olié et al, 2010

PAINFUL AND PROVOCATIVE EVENTS AND CAPABILITY FOR SUICIDE

•Men 18-39

 Measured pain tolerance to cold after playing violent or nonviolent video game



AREAS AFFECTED IN SUICIDE AND DEPRESSION



Treadway & Zald,, 2011

AREAS OF OVERLAP ACROSS DEPRESSION, SUICIDE, AND PAIN



SUICIDE BIOMARKERS STUDY: RESEARCH QUESTIONS

1. Is pain associated with capability for suicide?

- 2. What are the brain correlates of capability for suicide?
- 3. How are these brain correlates related to pain?

SAMPLE CRITERIA

MDD, Ideation/Attempt Controls History (n=20) (n=21) No psychiatric history Hamilton Depression Scale \geq 14 No lifetime use of Suicide ideation item ≥ 2 ٠ **MDD CONTROLS** psychotropics No borderline personality No medical conditions • Stable antidepressant >4 weeks No benzodiazepines/stimulants •

- 2 weeks prior to brain scan
- No unstable medical condition

STUDY METHODS



CLINICAL SCALES

- Suicide capability (Acquired Capability for Suicide Scale, <u>ACSS</u>)
- Suicidal ideation and attempt history (Columbia Suicide Rating Scale)

PAIN TASK: Cold Pressor Test





AREAS OF OVERLAP ACROSS DEPRESSION, SUICIDE, AND PAIN



BRAIN IMAGING

- Brain connectivity from 4 areas (regions of Interest)
- 2 parts of the insula (pain perception)
- 2 parts of the cingulate (emotional modulation of pain)
- Is brain connectivity associated with capability for suicide?



SAMPLE CHARACTERISTICS

	All MDD (n=20)	HC (n=21)
Age (y, Mean ± SD)	39.60 ± 13.34	42.48 ± 16.06
Sex (% female)	60.00%	47.62%
Education (y, Mean ± SD)	17.85 ± 2.50	18.75 ± 2.12
HAMD-17 (Mean ± SD) ***	18.45 ± 2.91	1.10 ± 1.34
QIDS-SR (Mean ± SD) ***	20.50 ± 6.33	$\textbf{2.14} \pm \textbf{2.03}$
Lifetime SI (1-5, Mean ± SD) ***	2.05 ± 1.57	0.05 ± 0.22
Current SI (1-5, Mean ± SD) ***	4.30 ± 1.03	0.05 ± 0.22
Lifetime SA (%)	70%	/
Lifetime NSSI (%)	45%	/

*** Between group difference is significant at the 0.001 level (2-tailed)

SUICIDE CAPABILITY IS ASSOCIATED WITH PAIN PROCESSING

	CS			CS
1. Number of past SA		Controlling	1. Number of past SA	
2. CS Total Score	-	for suicidal	2. CS Total Score	-
3. Pain Threshold (time)	0.24	ideation	3. Pain Threshold (time)	0.26
4. Pain Tolerance (time)	0.51*		4. Pain Tolerance (time)	0.52*
5. Endurance (time)	0.66**		5. Endurance (time)	0.66**
6. Pain Threshold			6. Pain Threshold	
(intensity)	-0.54		(intensity)	-0.55
7. Pain Tolerance	0.01		7. Pain Tolerance	0.07
(intensity)	-0.34		(intensity)	-0.3/
8. Intensity Change	0.40		8. Intensity Change	0.12

*. Correlation is significant at the 0.05 level (2-tailed), not significant after correction for multiple comparison **. Correlation is significant at the 0.01 level (2-tailed), significant after correction for multiple comparison

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6. Pain Threshold	-0.54*		6. Pain Threshold	
(intensity)			(intensity)	-0.557
7. Pain Tolerance	0.04		7. Pain Tolerance	0.07
(intensity)	-0.34		(intensity)	-0.3/
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BRAIN IMAGING REMINDER

- Brain connectivity from 4 areas (regions of Interest)
- 2 parts of the insula (pain perception)
- 2 parts of the cingulate (emotional modulation of pain)
- Is brain connectivity associated with capability for suicide?



SUICIDE CAPABILITY BRAIN CONNECTIVITY: POSTERIOR INSULA (pIC)





z = - 6.00

Z = - 2.00

Negative Correlation

pIC-PCG Connectivity

- pIC: intensity encoding, localization, learning of pain events (Coen et al, 2012; Bastuji et al, 2016)
 - PCG: cognitive and emotional processing
- Suicidal ideation, self-harm (Dimick et al, 2021; Liu et al, 2021)

Right paracingulate gyrus (PCG)

(12, 44, -2, near ventral ACC)

Z-max = -4.42 z threshold = 3.0 p = 0.018, voxels = 100

SUICIDE CAPABILITY BRAIN CONNECTIVITY: ANTERIOR INSULA (aIC)







SUICIDE CAPABILITY BRAIN CONNECTIVITY: ANTERIOR MIDCINGULATE (aMCC)







Z-max = 4.00, z threshold = 3.0 p = 0.036 voxels = 95

SUICIDE CAPABILITY BRAIN CONNECTIVITY: SUBGENUAL ANTERIOR CINGULATE (sgACC)







p = 0.022 voxels = 90

BRAIN CONNECTIVITY OF SUICIDE CAPABILITY SUMMARY



OVERVIEW OF PAIN RESULTS

• Behavioural pain may be objective marker of capability for suicide

• Brain correlates of suicide capability overlap with essential pain networks

WHAT ARE THE NEXT STEPS?

- •Need better understanding of neurobiology of pain in suicide risk
- Stability of suicide pain markers
- Implication for developing objective tests for risk assessment
- Implication for therapeutics?

INTERVENTIONS FOR SUICIDE RISK



THE AMERICAN JOURNAL OF PSYCHIATRY

Ketamine for Rapid Reduction of Suicidal Thoughts in Major Depression: A Midazolam-Controlled Randomized Clinical Trial

Ketamine blocks glutamate, rapid acting



Time Point

Grunebaum et al, 2017

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION REDUCES SUICIDAL IDEATION



Weissman et al, 2018

BRIEF SKILLS FOR SAFER LIVING (B-SfSL)

4 main tasks:

- Understanding individual's suicidal experience
- 2. Skills building
- 3. Developing a safety plan
- 4. Identifying obstacles to enacting the safety plan



Rizvi et al, data on file

Understand your biases and stigma

MYTH "Once a person attempts suicide, they won't do it again."

MYTH

"People who talk about suicide don't do it."

MYTH

"Non-fatal attempts are only attention seeking behaviours."

•Understand your biases

Name it to tame it



Understand your biases

Name it to tame it

YouthLine A SERVICE OF Sines Alife A SERVICE OF Ines Alife A ST7.968.8491 teen2teen to 839863

National Crisis Hotline: 800-273-8255 or Text "4hope" to 741741

Educate yourself and know your resources



- Understand your biases
- Name it to tame it
- •Educate yourself and know your resources
- •Open and nonjudgmental communication



- Understand your biases
- •Honor feelings!
- •Educate yourself and know your resources
- Open and nonjudgmental communication



Get support from a professional

WHAT CAN YOU DO IF A FRIEND/FAMILY MEMBER HAS SUICIDAL THOUGHTS?

DO

- Assess warning signs
 - No hope, means, withdrawal
- Speak up
 - "Are you having thoughts of suicide?"
- Active listening

DON'T

•Argue

- "You have so much to live for," "Your suicide will hurt your family"
- Lecture on value of life
- Promise confidentiality
- •Problem fixing
- •Blame yourself

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KEY TAKEAWAYS AND RESOURCES

- Suicide is not about wanting to die
- Factors related to suicide risk are complex
- Pain processing in the brain may be an important marker of risk
- Vital to build community of support



Available on Amazon

PAIN THRESHOLD INTENSITY

