

The background of the slide is a dark space scene. In the foreground, the curved horizon of the planet Mars is visible, showing its reddish-brown surface with darker patches. Above the horizon, a bright sun or star is visible, creating a lens flare effect. In the upper right corner, a small satellite or space probe is seen, with a prominent blue parabolic dish antenna and other instruments.

# New horizon: Ketamine for Suicidal Ideation: An Emergency Department Intervention

*דר' יואב דומני*

*סגן מנהל מחלקה פסיכיאטרית ג'*

*מרכז רפואי ע"ש חיים שיבא.*

*יום העיון של האיגוד לפסיכיאטריה ביולוגית - 27.11.19*

# Conflict Of Interests

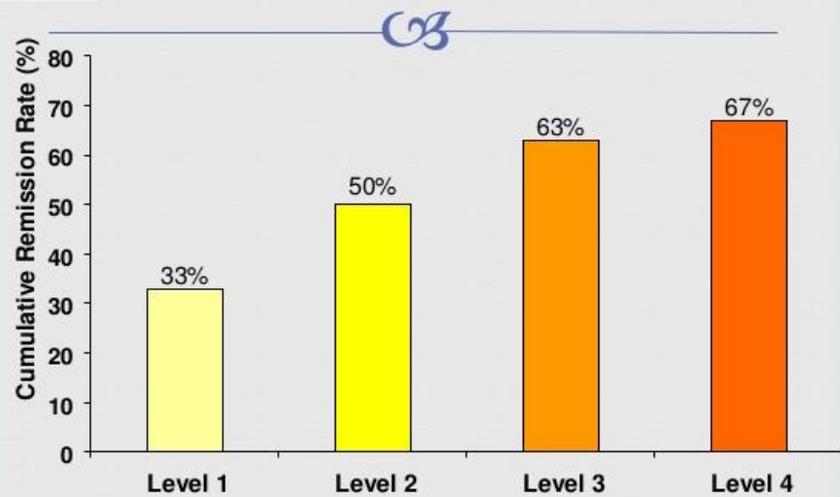
- Advisory board- Janssen.

# Treatment for depression is not satisfactory

- Treatment Resistant Depression.
- No breakthroughs in depression treatments for over 40 years.



STAR\*D Cumulative Remission Rates



Gaynes B, et al. *Clev Clin J Med*. 2008;75(1):57-65.

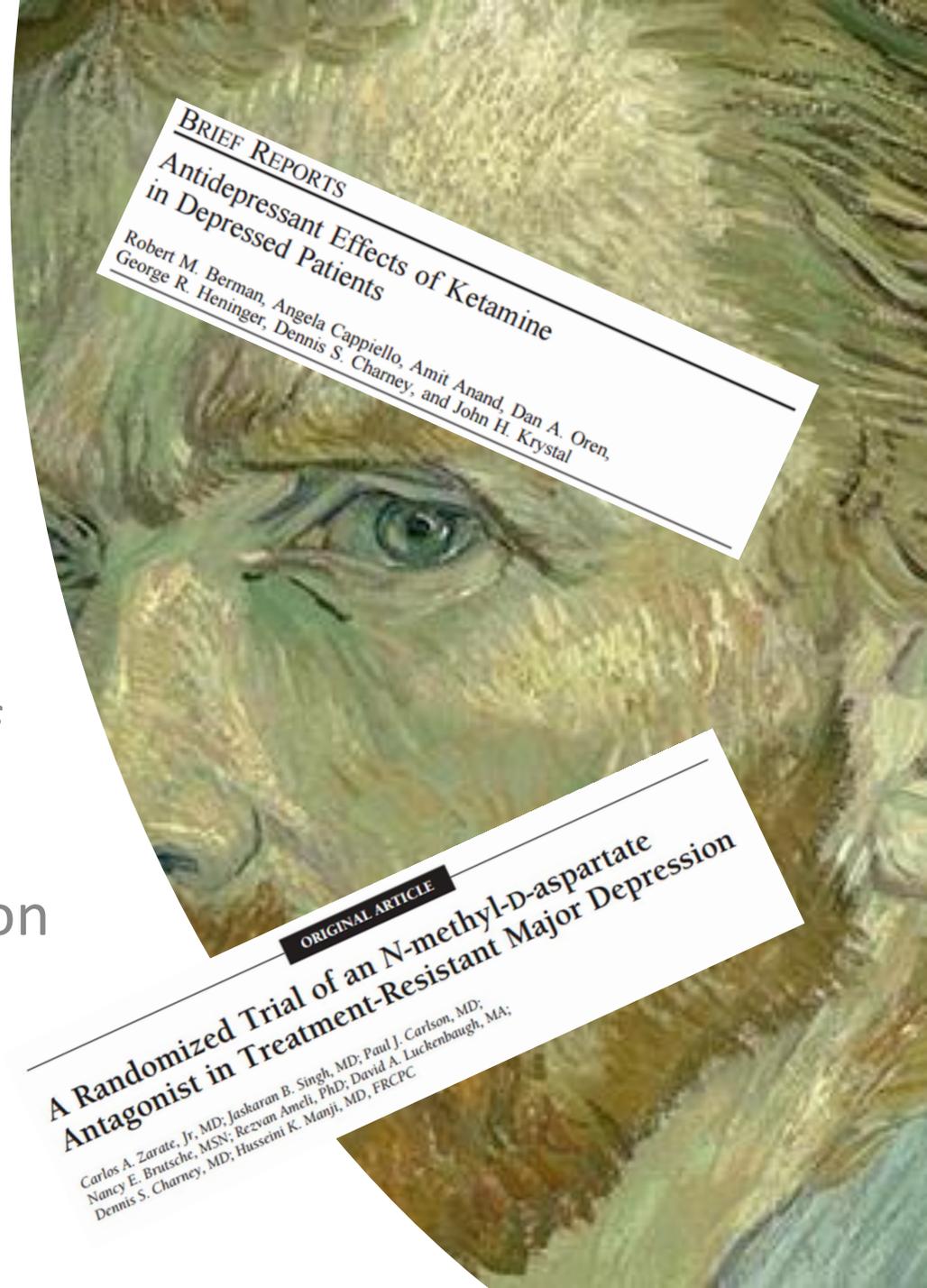
A dark, irregular ink blot with white text. The blot is centered on a white background and has a rough, splattered edge. The text is white and centered within the blot.

And then came  
ketamine

# Ketamine for depression

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- In 2000 Berman et al published the first evidence of the antidepressant effect of ketamine.
- In 2006, Zarate et-al published the first RCT on ketamine for TRD.
- This study is my inspiration



# Mechanism of action

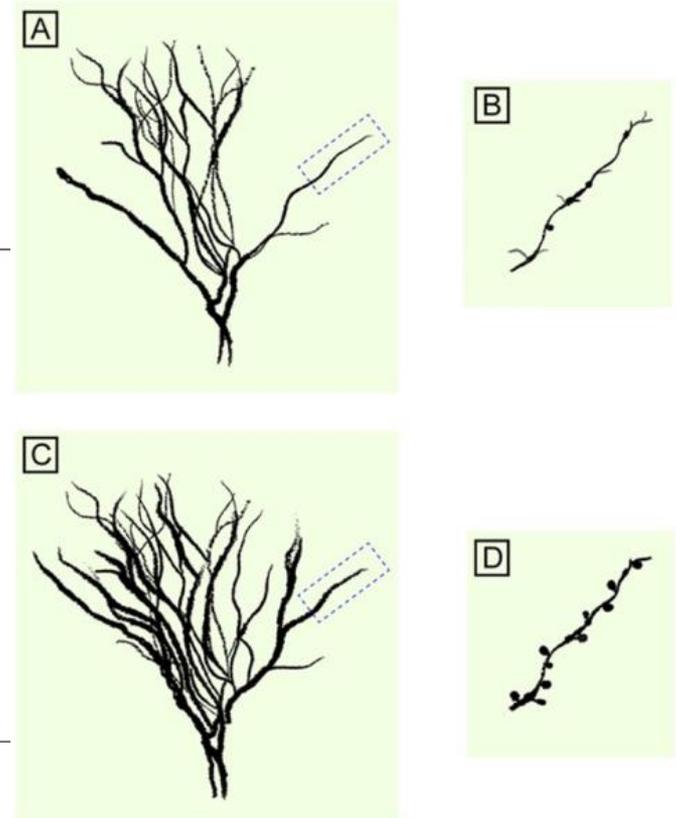
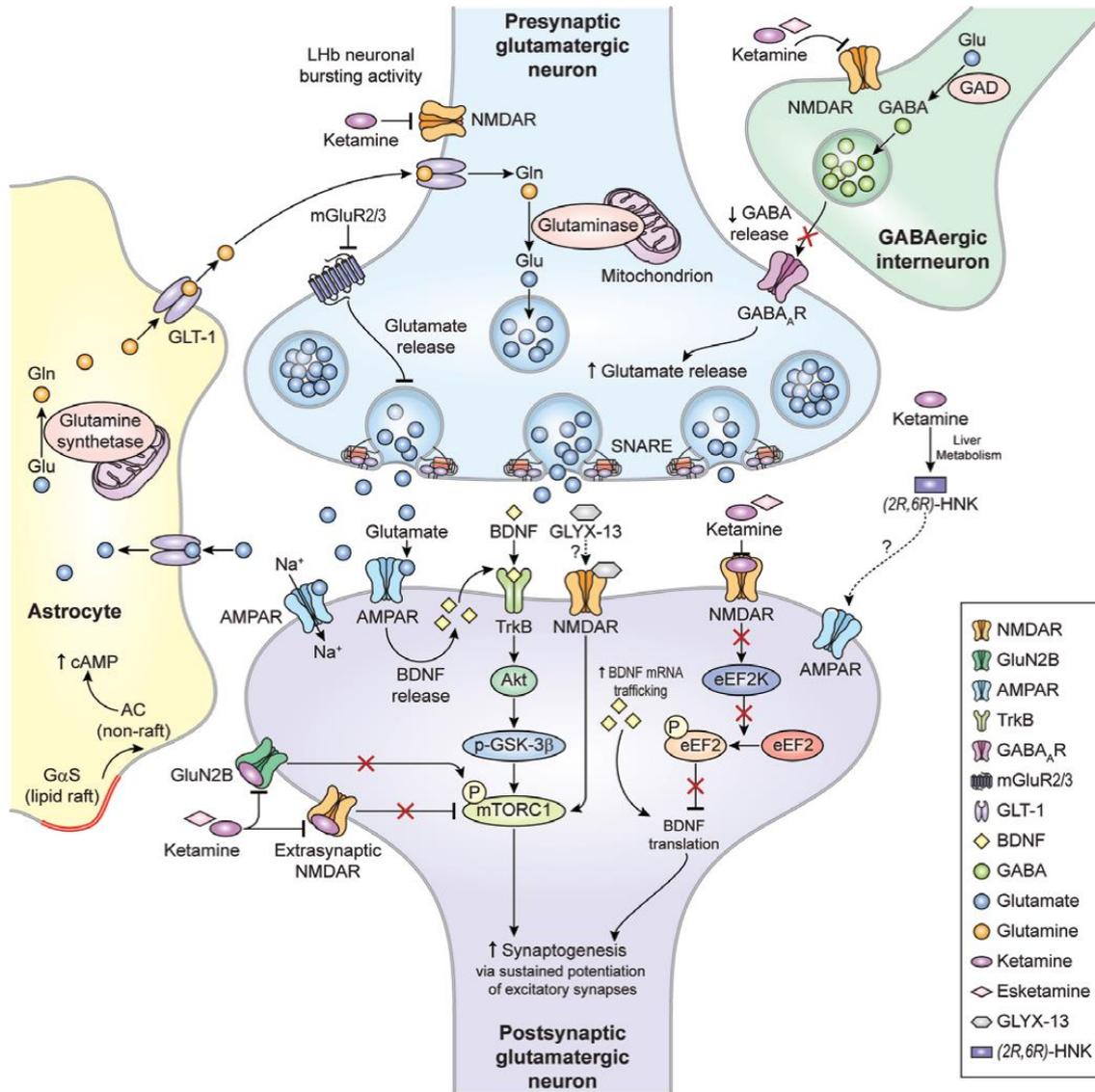
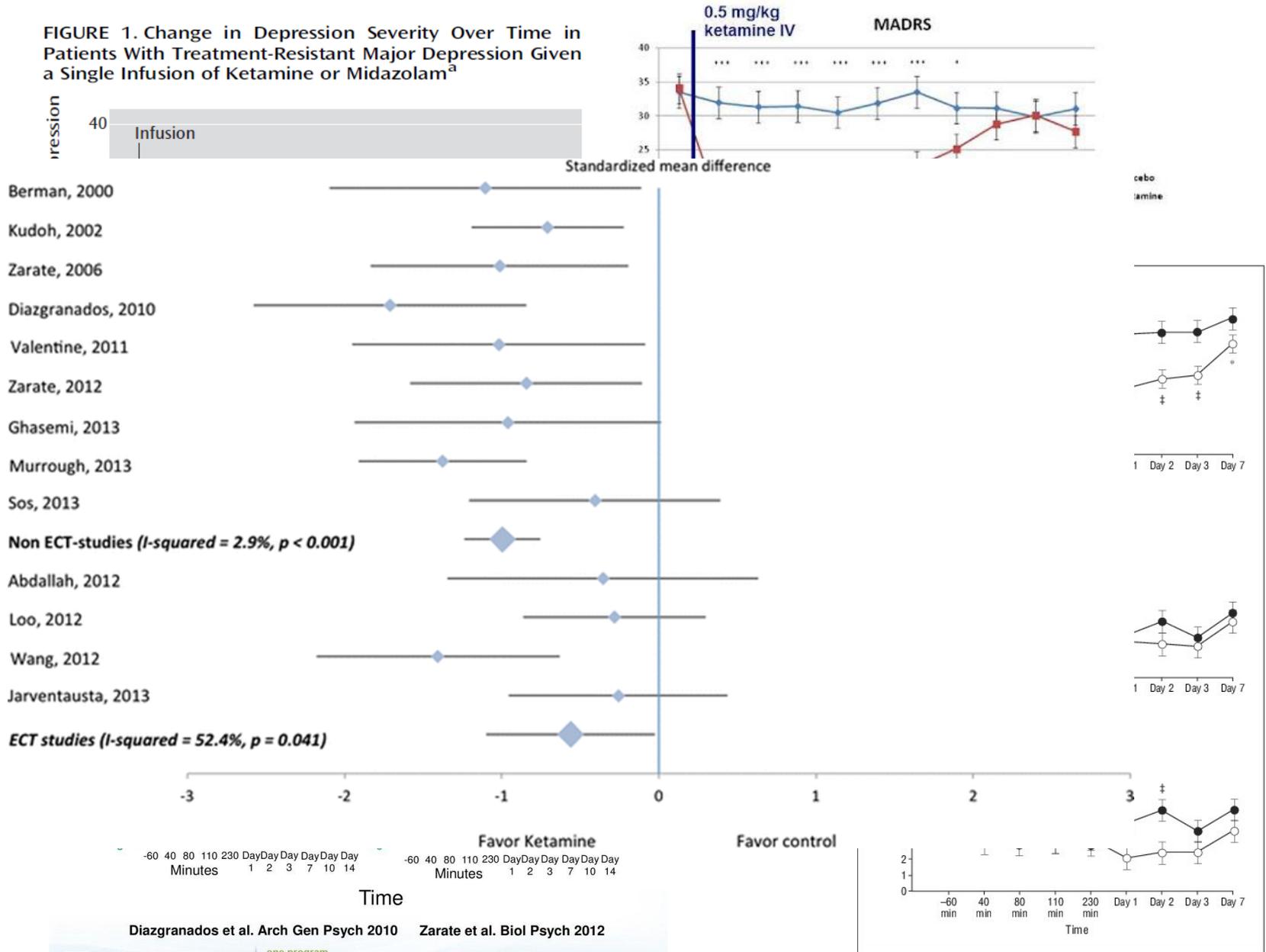


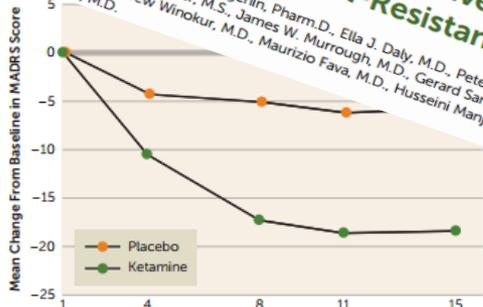
FIGURE 1. Change in Depression Severity Over Time in Patients With Treatment-Resistant Major Depression Given a Single Infusion of Ketamine or Midazolam<sup>a</sup>



# Repeated dosage

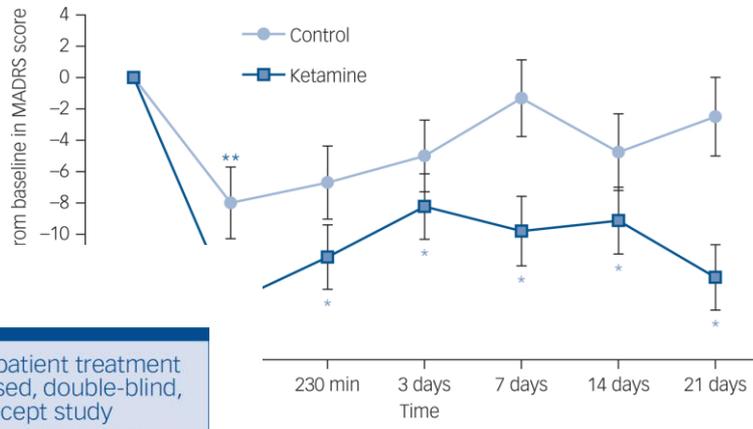
## A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients With Treatment-Resistant Depression

Jaskaran B. Singh, M.D., Maggie Fedgchin, Pharm.D., Ella J. Daly, M.D., Peter De Boer, Ph.D., Kimberly Cooper, M.S., Pilar Lim, Ph.D., Christine Pinter, M.S., James W. Murrough, M.D., Gerard Sanacora, M.D., Richard C. Shelton, M.D., Benji Kunian, M.D., Andrew Winokur, M.D., Maurizio Fava, M.D., Hussein Marji, M.D., Wayne C. Drevets, M.D., Luc Van Nueten, M.D.



Number of Patients:	1	4	8	11	15
Placebo	16	15	13	13	13
Ketamine	18	17	15	16	16

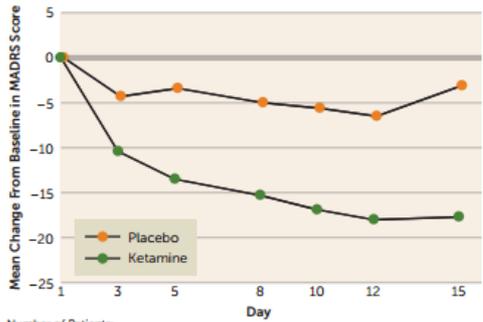
BJPsych The British Journal of Psychiatry (2018) Page 1 of 7. doi: 10.1192/bjp.2018.196



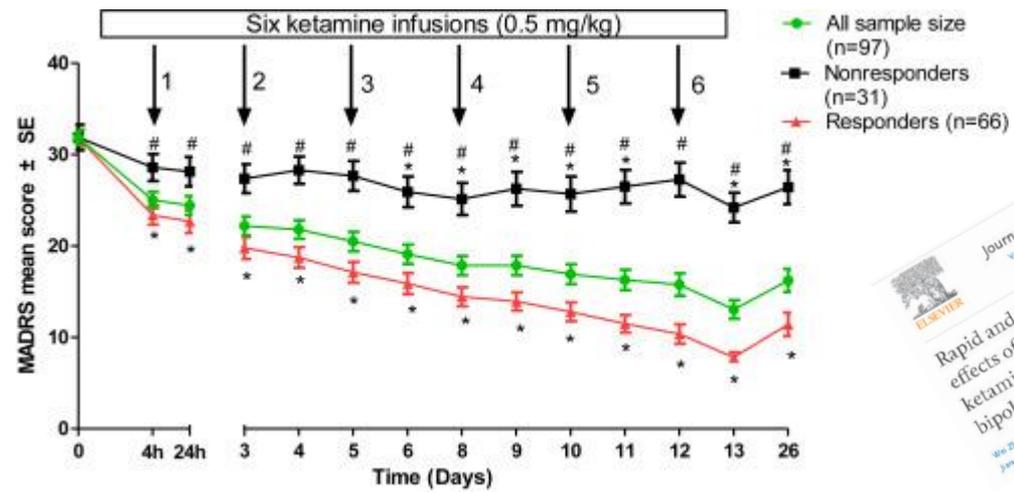
Repeated oral ketamine for out-patient treatment of resistant depression: randomised, double-blind, placebo-controlled, proof-of-concept study  
 Yoav Domyan\*, Maya Bleich-Cohen\*, Ricardo Tarrasch, Roi Meidan, Olga Litvak-Lazar, Nadav Stopplerman, Shaul Schreiber, Miki Bloch, Talma Hendler and Haggai Sharon

Background The reduction in MADRS score on day 21 was 12.75 in the

### B. Thrice-Weekly Dosing



Number of Patients:	1	3	5	8	10	12	15
Placebo	16	16	15	16	16	14	16
Ketamine	17	17	13	16	16	11	13

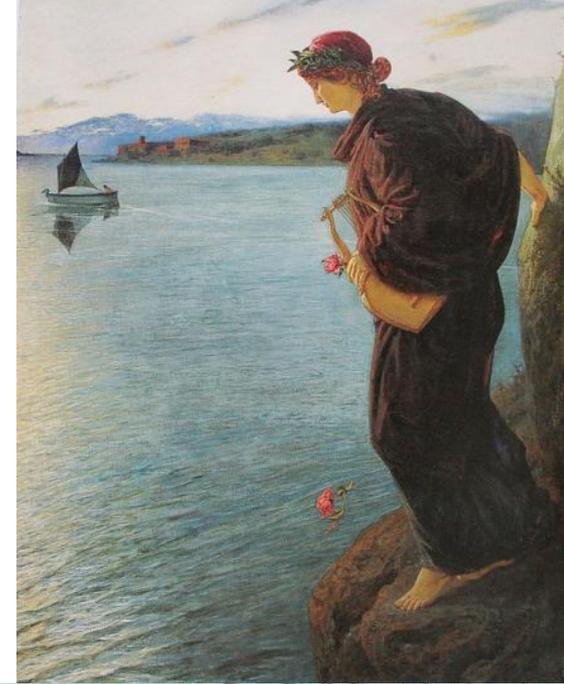


Journal of Psychiatric Research  
 Volume 126, November 2018, Pages 61-68  
 Rapid and longer-term antidepressant effects of repeated-dose intravenous ketamine for patients with unipolar and bipolar depression  
 Wu Zhang\*, Yan Ling Zhou\*, Wei Jian Liu\*, Cheng-Yu Wang\*, Yan-Yu Zhou\*, Han-Qi Li\*, Li-Jian Chen\*, Ming-Ding Li\*, Yu-Ping Song \* & Q

# Ketamine for depression

- There is a well established rapid, temporary, antidepressant effects of a single IV ketamine for depression, which is safe and well tolerated.
- Safety of Repeated IV ketamine are not well characterized
- Concerns have been raised about its dissociative side effects and risk of abuse.
- Treatment guidelines are needed.

# Suicide

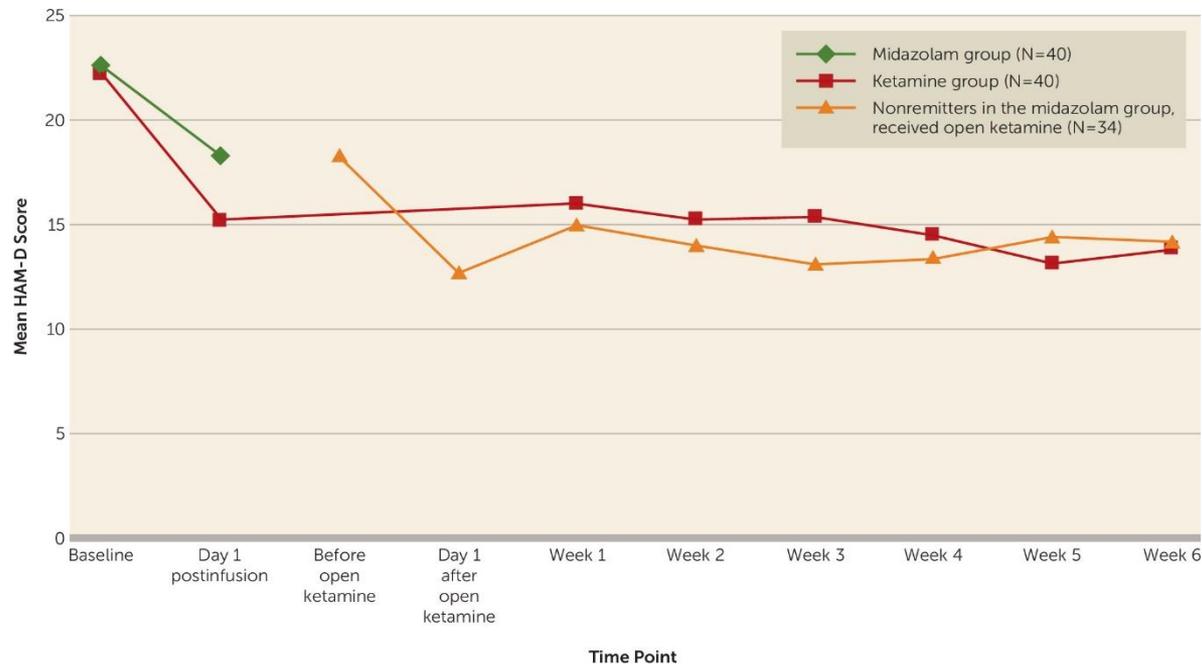




And then came  
ketamine

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

American Journal of Psychiatry

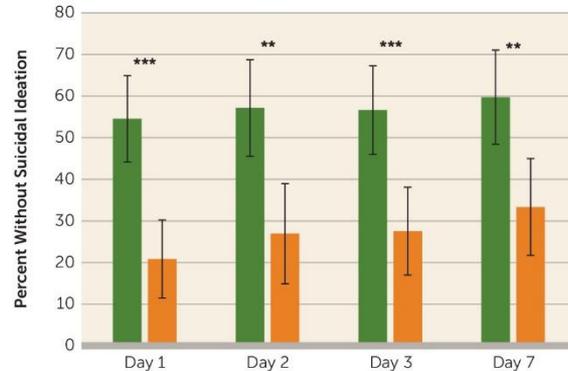


a The data are based on the modified intent-to-treat sample (N=40 per group). Score on the 17-Item Hamilton Depression Rating Scale (HAM-D) 24 hours after infusion (day 1) was a secondary outcome measure. Remission was defined as a Scale for Suicidal Ideation score  $\geq 50\%$  below baseline at day 1 and less than the study eligibility threshold of 4. For nonremitters, the blind was broken and patients who were allocated to midazolam were offered an open ketamine infusion, usually the following day. The reduction in HAM-D score was greater in the ketamine group compared with the midazolam group, but the difference fell short of statistical significance ( $p=0.06$ ).

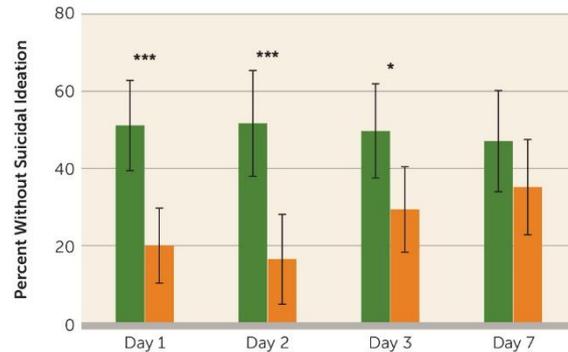
# From: The Effect of a Single Dose of Intravenous Ketamine on Suicidal Ideation: A Systematic Review and Individual Participant Data Meta-Analysis

American Journal of Psychiatry

## A. Clinician-Administered Measures

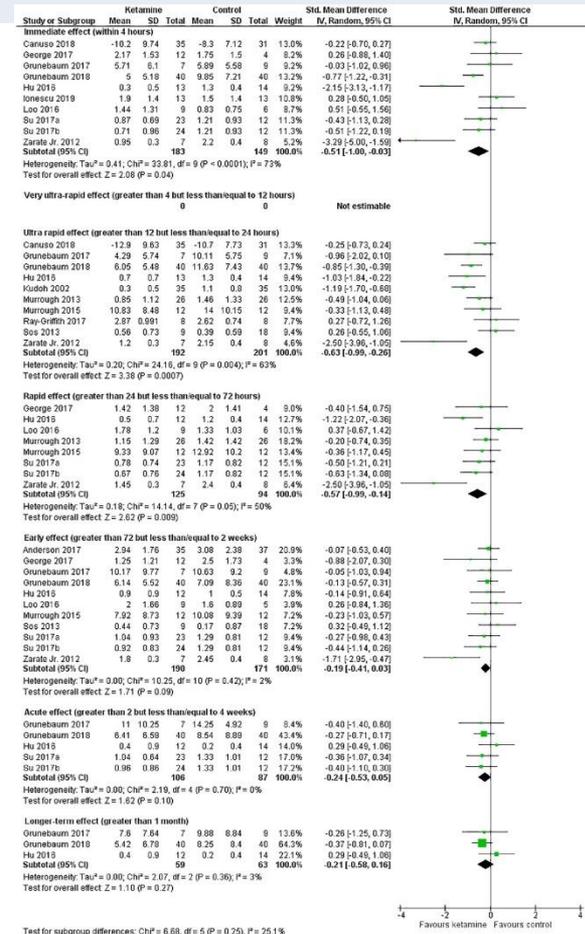


## B. Self-Report Measures



\* $p < 0.05$ . \*\* $p < 0.01$ . \*\*\* $p < 0.001$ .

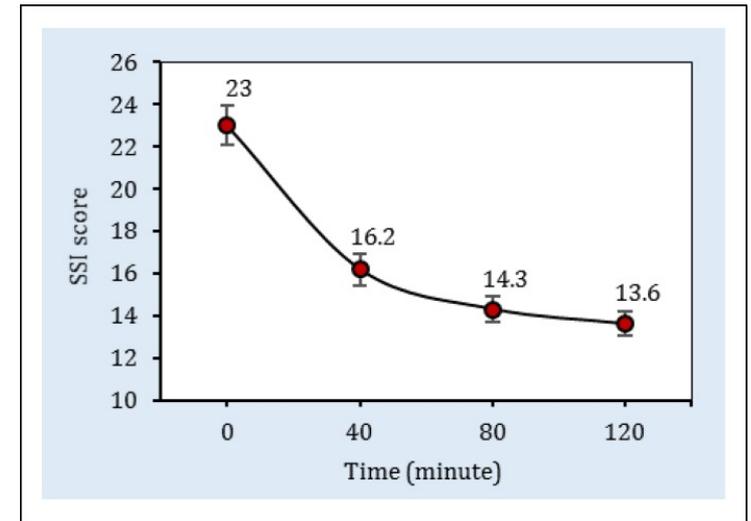
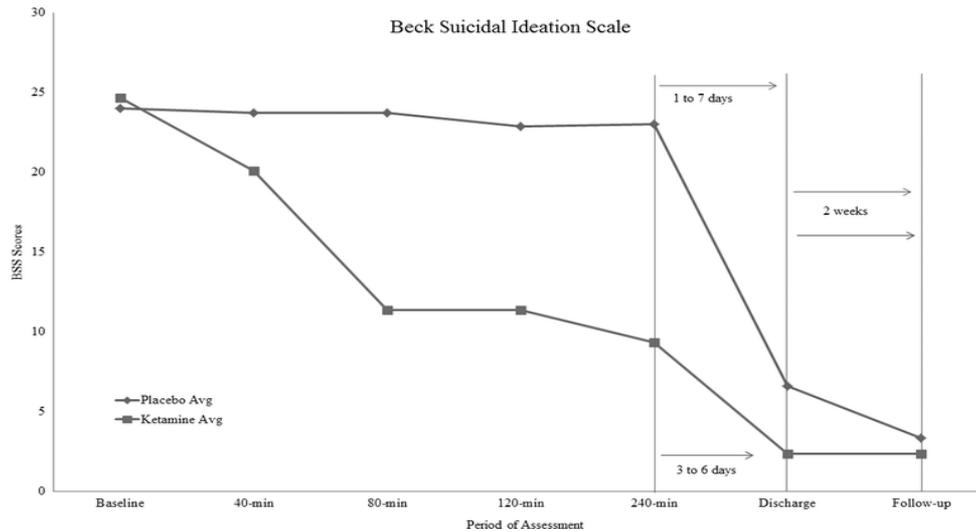
■ Ketamine  
■ Control



# Suicide ideation in Emergency departments

- Depressed patients are often presenting to the emergency department with complaints of suicidal thoughts
- Half a million admissions annually to the emergency department in the USA
- No rapid treatments
- There is an urgent need to pursue treatment options for SI in the ED.

**FIGURE 1.** Average scores on the BSS for placebo versus ketamine over time.



RESEARCH ARTICLE

# Ketamine for acute suicidal ideation. An emergency department intervention: A randomized, double-blind, placebo-controlled, proof-of-concept trial

Yoav Domany , Richard C. Shelton, Cheryl B. McCullumsmith

First published: 16 November 2019 | <https://doi.org/10.1002/da.22975>

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# PSYCHIATRIC NEWS

# ALERT

### Current Issue



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Tuesday, November 19, 2019

## Ketamine Found to Rapidly Reduce Suicidal Thoughts in Depressed, Suicidal Patients in ER



Patients presenting to an emergency room with complaints of suicidal thoughts may experience relief from these thoughts within 90 minutes of a single, low-dose infusion of ketamine, suggests a [small study](#) in *Depression & Anxiety*.

While previous studies have demonstrated the potential of ketamine to reduce suicidal thoughts in patients with depression (including this [2017 paper](#) published in the *American Journal of Psychiatry*), this new study examined the effectiveness of a low-dose infusion administered in an emergency department. "A single infusion of ketamine, administered in the emergency department, is a safe and feasible treatment option for

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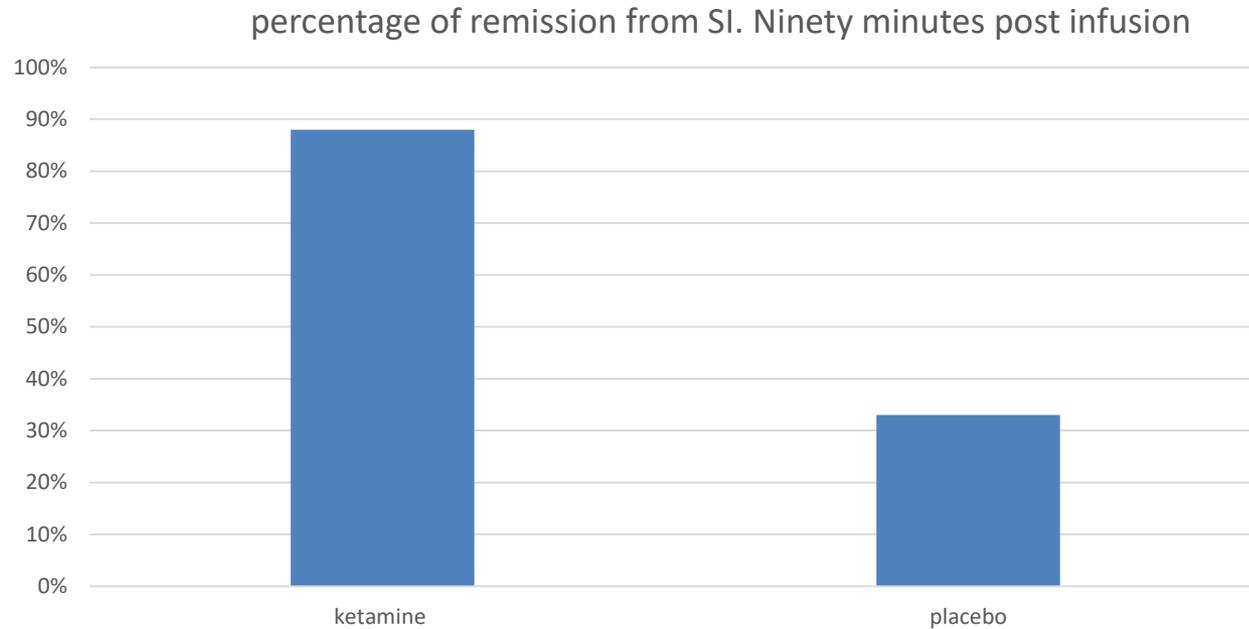
# Methods

- Randomized, double-blind, placebo-controlled, proof-of-concept trial,
- Eighteen depressed participants with acute suicidal ideation and required hospitalization.
- They were randomized to either intravenous ketamine 0.2mg/kg or saline placebo.

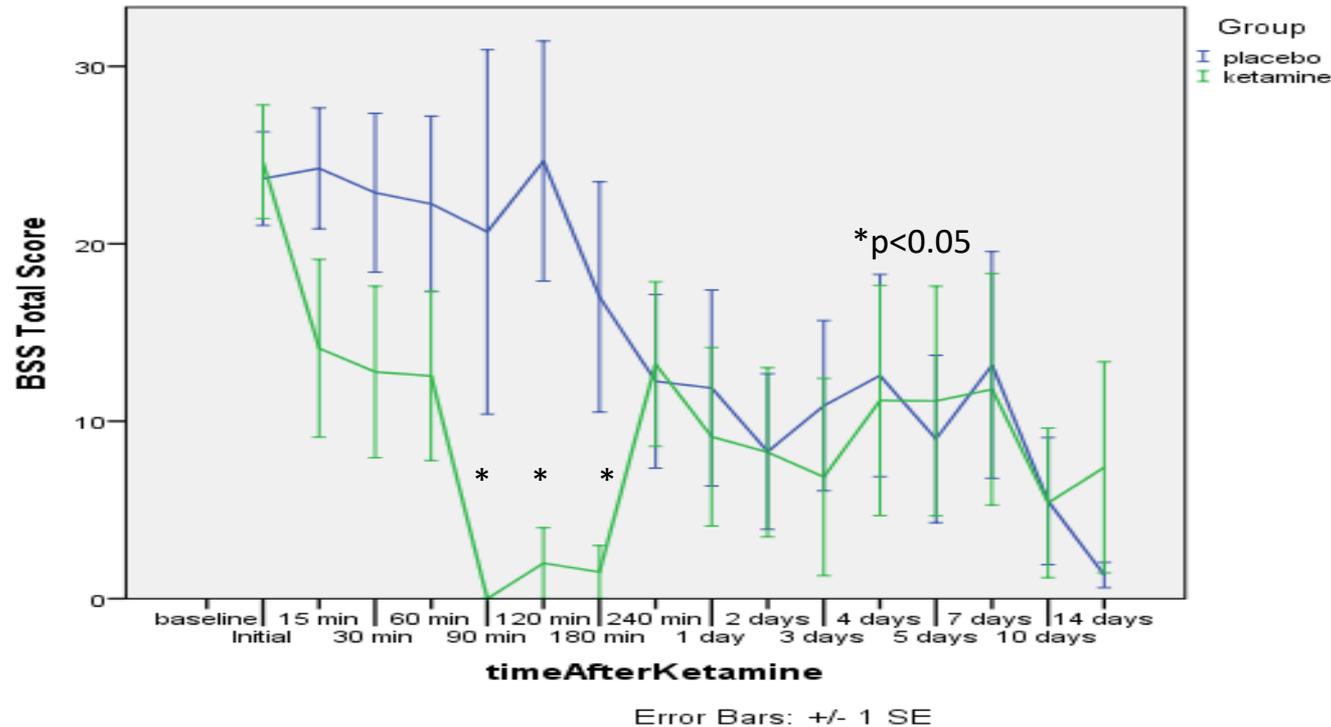
# Methods

- Safety and efficacy evaluations were scheduled for 15, 30, 60, 90, 120, 180 and 240 minutes, and on days 1, 2, 3, 7, and 14 post infusion.
- The main outcome was suicidal ideation, with secondary measures of depression.

# Results: Remission from SI.



# Results- Suicidal ideation across time



- Ketamine administration in the ED setting alleviated SI over placebo at 90-180 minutes post administration.

# Novelty

- We hypothesize that suicide ideation can be addressed as distinct domains.
  - A. Hopelessness
  - B. Pessimistic thoughts
  - C. Anxiety
  - D. Impulsivity
  - The different effect ketamine might have.

# Novelty

- RDoC approach
- Examination of these neurobiological domains is a novel perspective that may give additional insights into both ketamine's unique actions and the neurobiological underpinnings of SI
- Characterize the mechanism underneath this lethal condition.
- Suicide related brain dysfunction

# Results- Suicide Related RDoC Constructs

- A: Hopelessness
- B: Pessimistic thoughts
- C: Anxiety
- D: Impulsivity

We found ketamine to improve negative and positive valance systems but not cognitive systems.

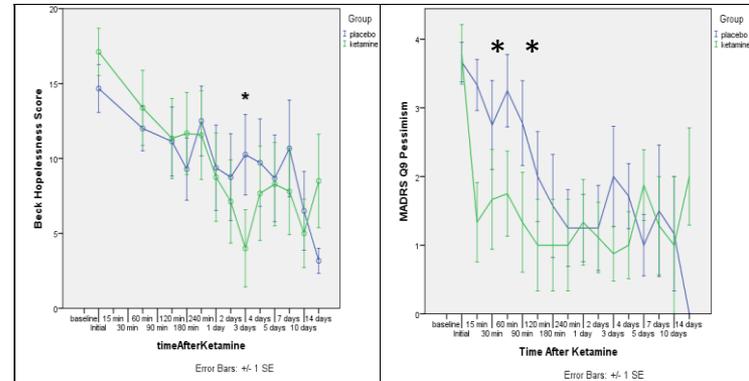


Figure 3a: Change in BHS across time, as a measure of hopelessness. BHS- Beck Hopelessness Scale.\*  $p < 0.05$

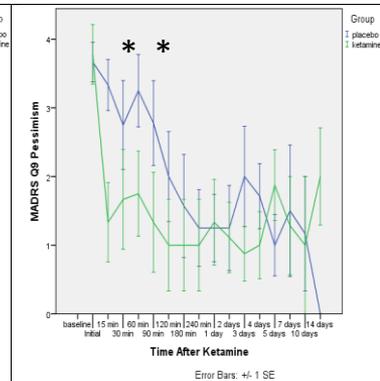


Figure 3b: Change in MADRS 9<sup>th</sup> question across time, as a measure of pessimistic thoughts. MADRS Montgomery Asberg Depression Rating Scale.\*  $p < 0.05$

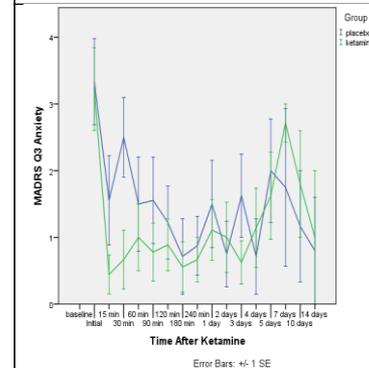


Figure 3c: Change in MADRS 3<sup>rd</sup> question across time, as a measure of Inner tension. MADRS Montgomery Asberg Depression Rating Scale.\*  $p < 0.05$

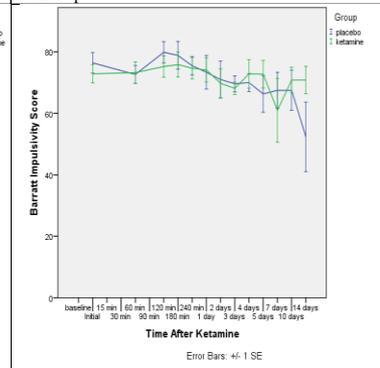


Figure 3d: Change in BIS question across time, as a measure of impulsivity. No difference was evident between ketamine and placebo. BIS Barrett Impulsivity Score.

# Conclusion

- Ketamine is a safe and feasible treatment option in the ED settings for depressed patients with acute SI.
- Ketamine alleviated SI in the first hours post infusion.
- The use of low dose ketamine for suicidal individuals deserves serious consideration as a suicide prevention measure
- We present here an RDoC based, novel research paradigm, for suicide research.

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# Case Study

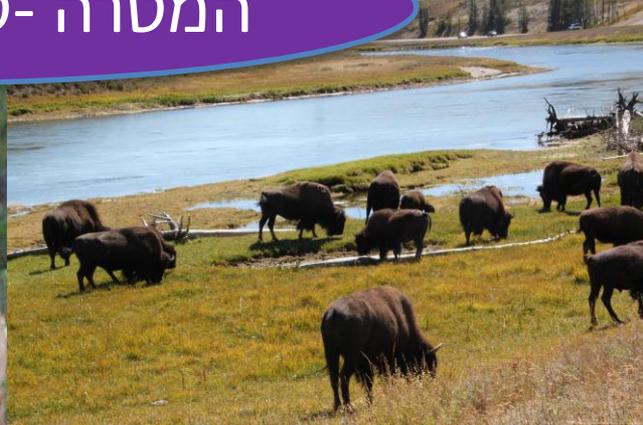
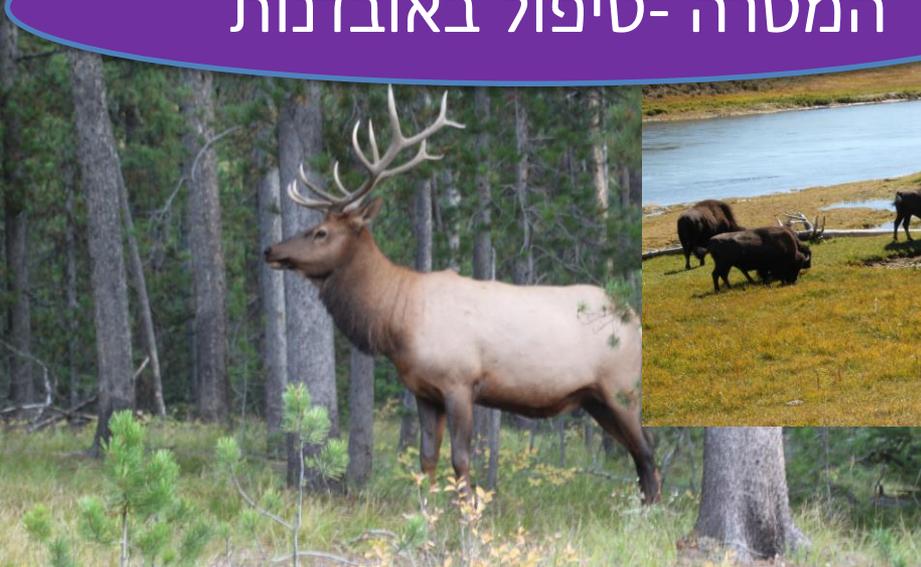
# אולי עוד מילה על רגשות.

- הספק
- התצפית
- המדע
- הקסם

# תודה על ההקשבה



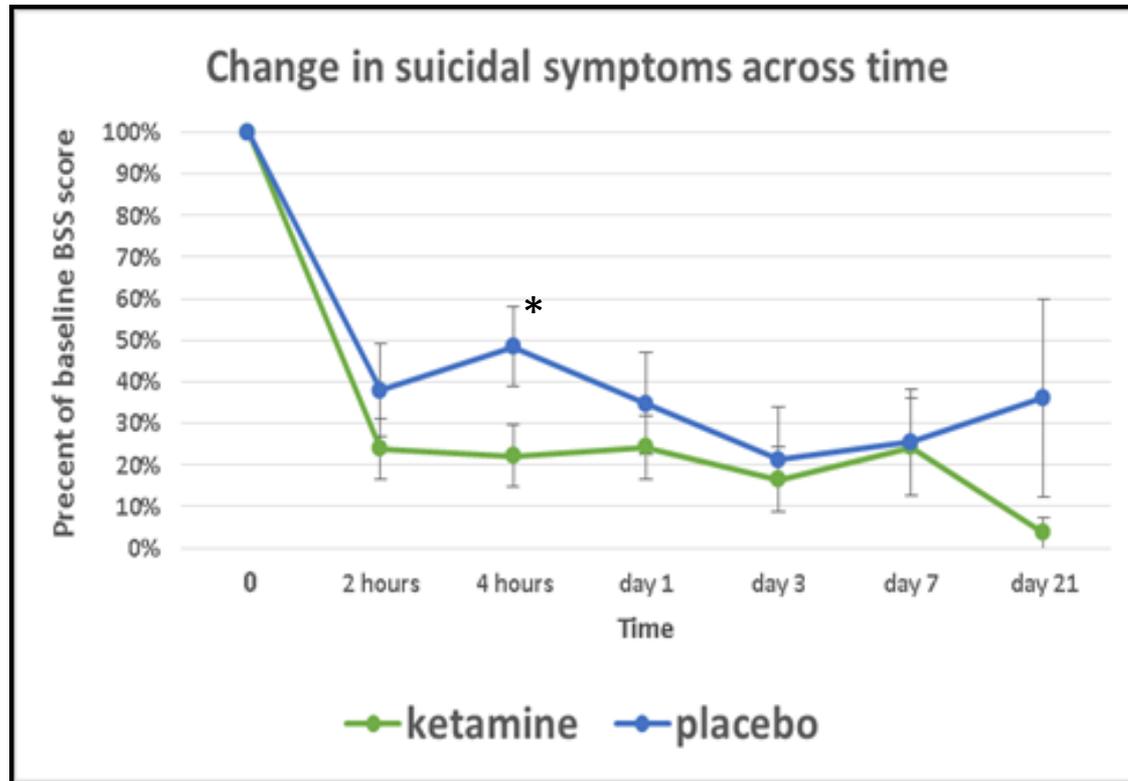
המטרה - טיפול באובדנות



# ABC of suicide prevention

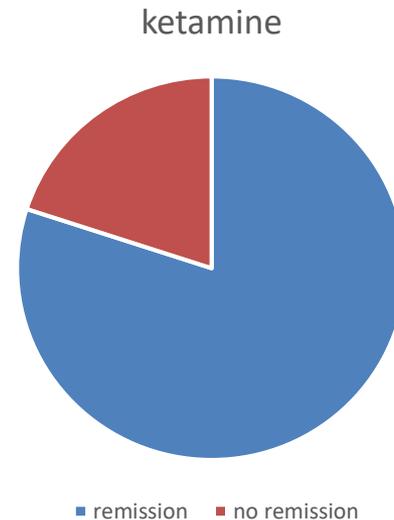
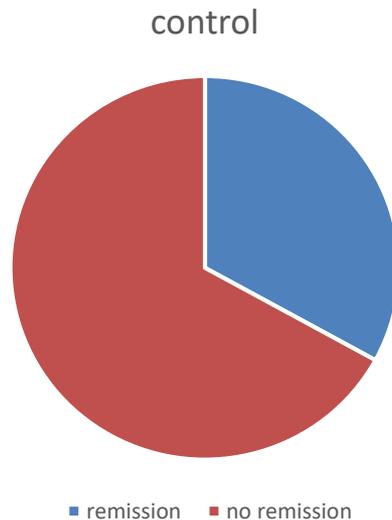
- Safety
  - A- Acknowledgement/ Ask
  - B- Build confidence
  - C- Care
    - טיפול
    - איכפתיות-אמפטיה
    - דאגה

# תוצאות טיפול בקטמין מפחית חשיבה אובדנית

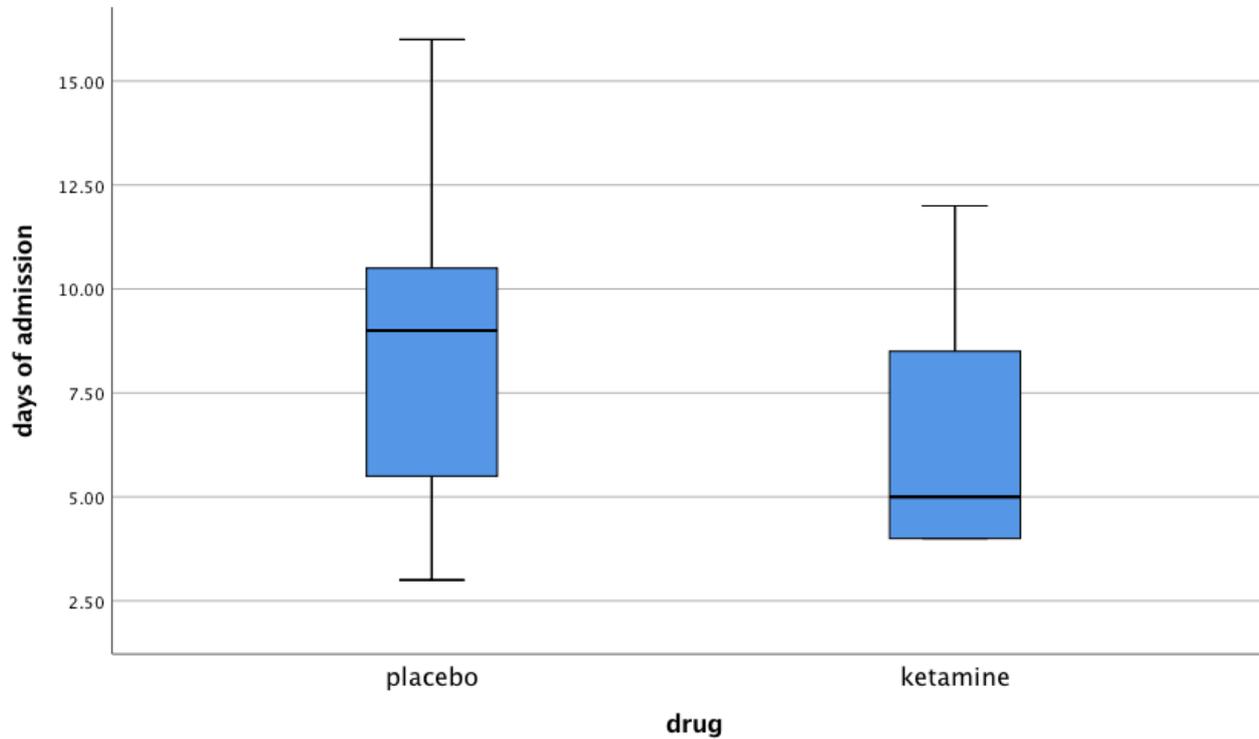


# Results- Remission

- Remission from SI as defined by a score of 0 on the MADRS-SI item (indicating no suicidal thoughts). ( $p < 0.01$ )



# Results- days of hospitalization



# Conclusion

- Ketamine alleviated acute SI and improved depressive symptoms four hours post drug administration in extremely suicidal cohort.
- Our findings supports a trans-diagnostic approach for SI care.
- **Ketamine for suicidal individuals deserves serious consideration as a suicide prevention measure.**