Jenny Berrío & Otto Kalliokoski

FIGHTING IRREPRODUCIBILITY IN PRECLINICAL NEUROSCIENCE USING A META-ANALYTICAL APPROACH

The case of the Chronic Unpredictable Stress model of depression

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CONFLICT OF INTEREST DISCLOSURE

We have NO potential conflict of interest to report

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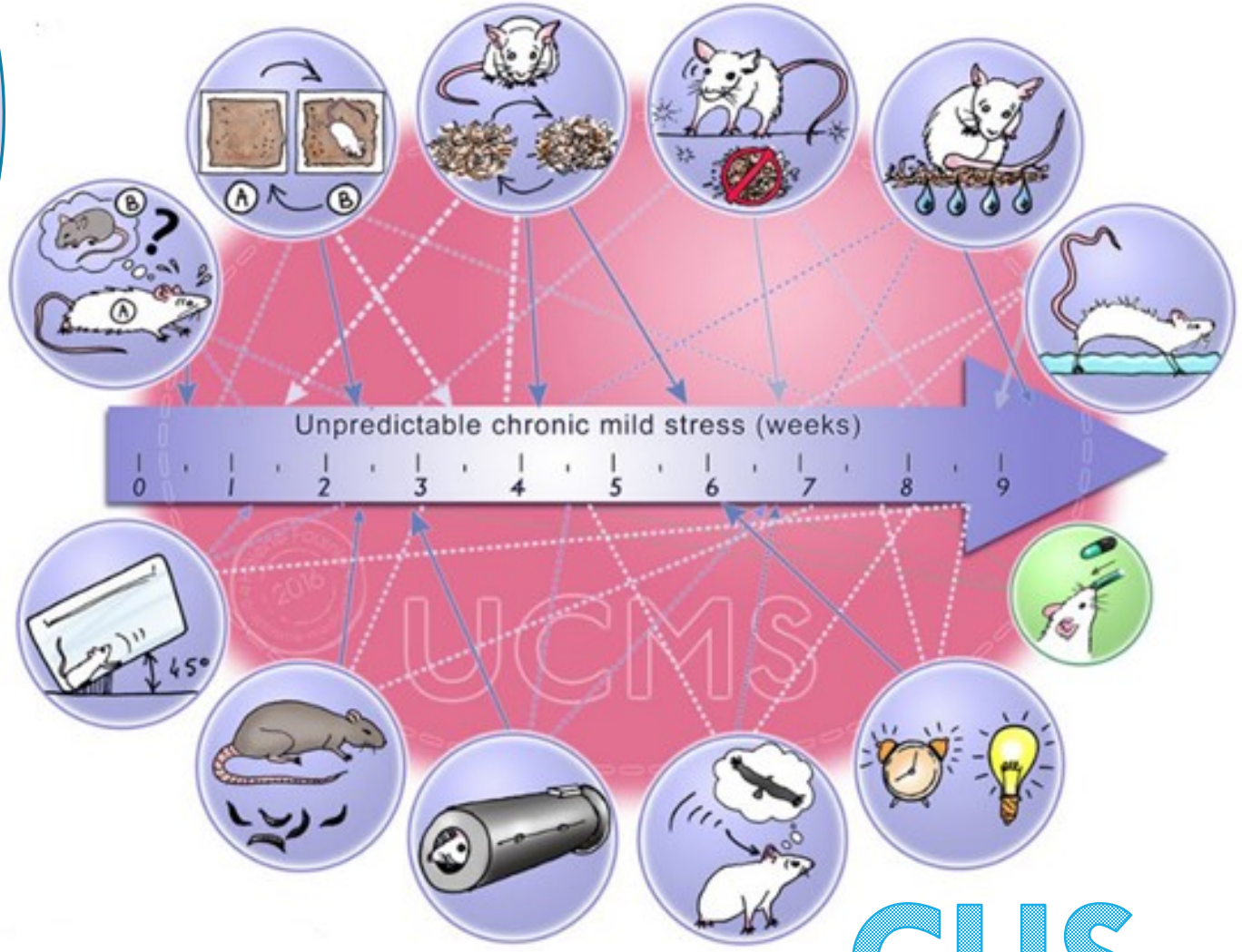


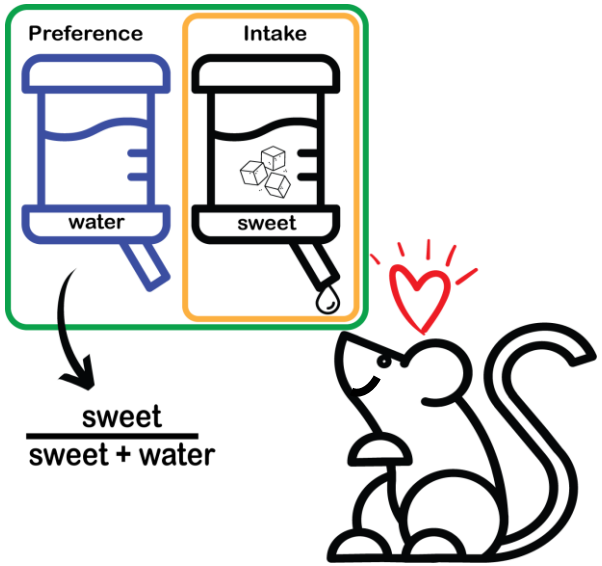
Depression

CUS

(Katz, 1982; P. Willner et al., 1987)

Image sources : https://www.linkedin.com/pulse/chronic-stress-lets-talk-jonny-atter/; Planchez et al, 2019

Anhedonia : Decreased ability to feel pleasure and reduced interest in activities an individual used to enjoy



Animal's consumption of sweetened solution

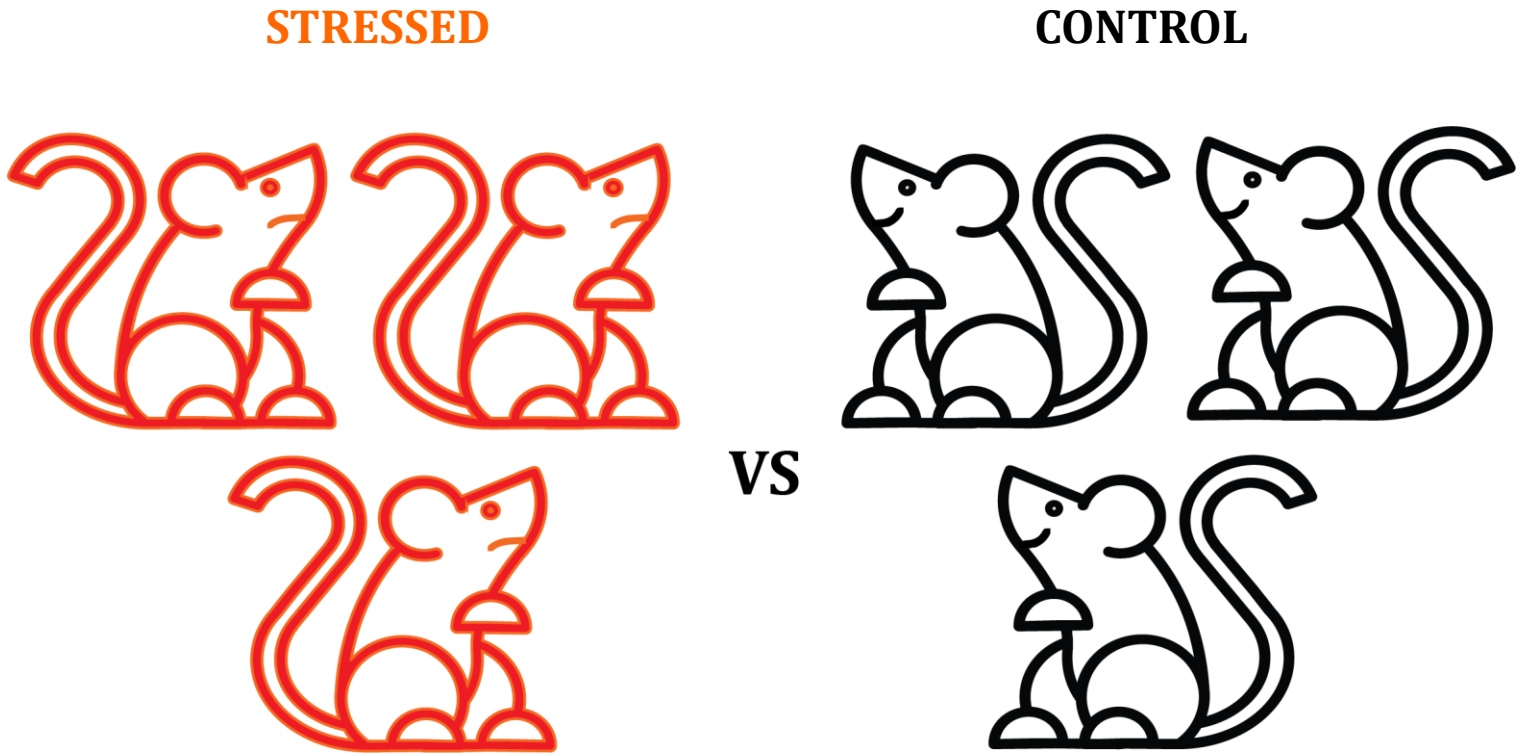
SUCROSE PREFERENCE TEST (SPT)

Level of the stimulation (threshold)

INTRACRANIAL SELF-STIMULATION (ICSS)

Images created with icons from https://thenounproject.com/

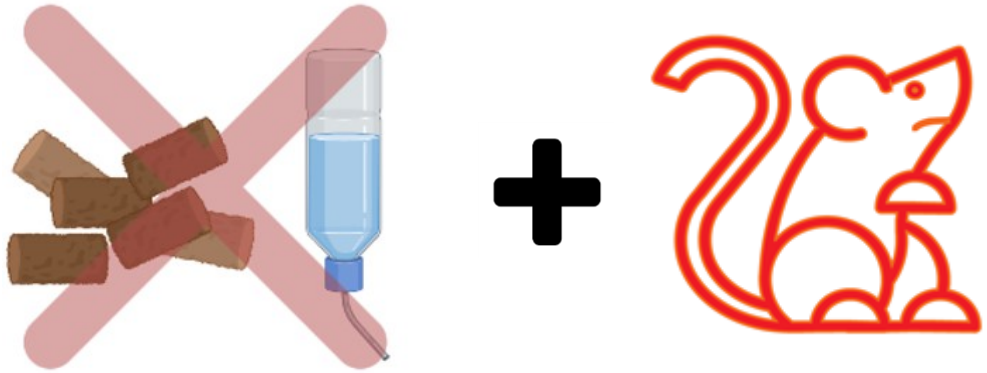
Expected outcomes



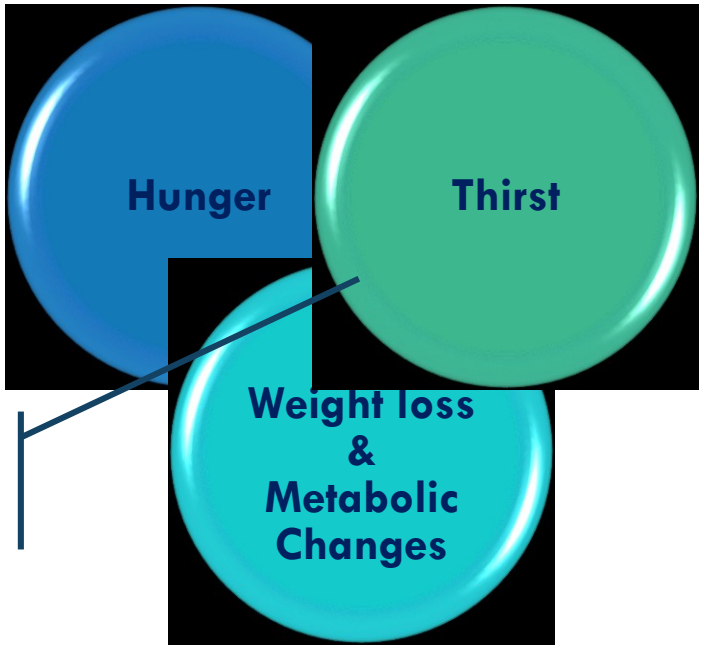
Anhedonia =

SPT	ICSS
DECREASED SWEET CONSUMPTION	INCREASED STIMULATION THRESHOLD

Lack of reproducibility and inconsistency in results



Liking of **caloric solution**



What Are We Really Measuring?

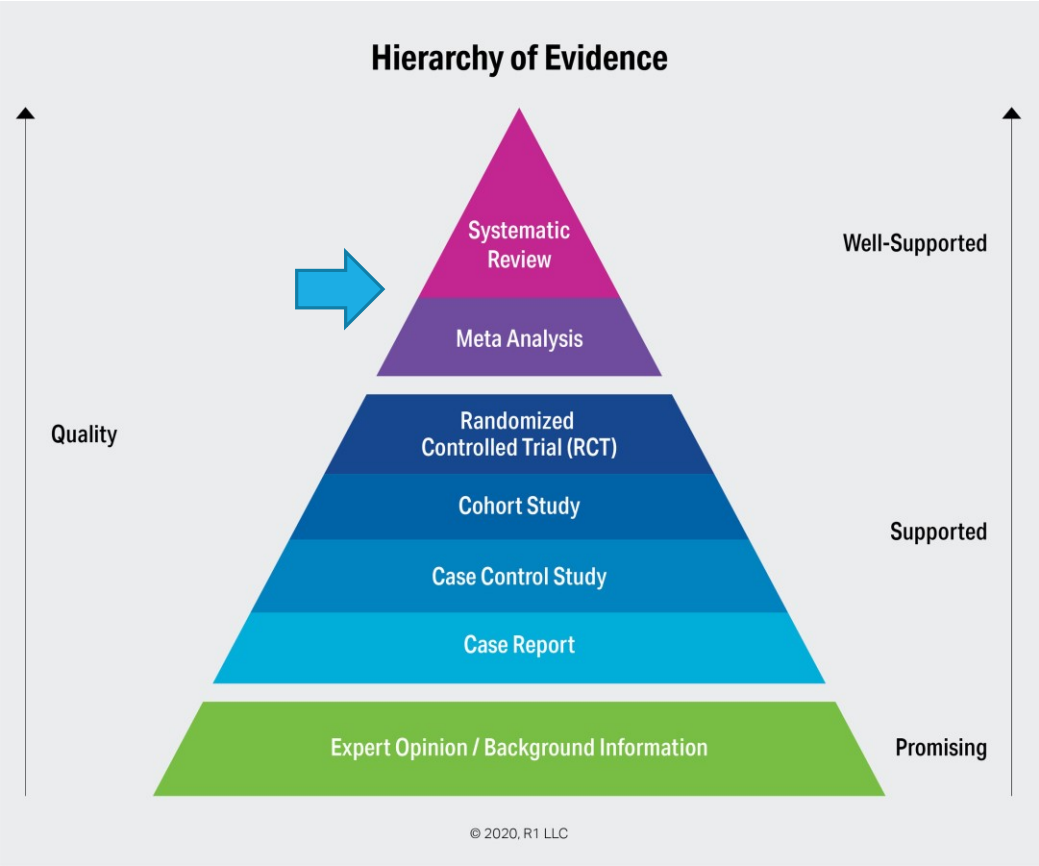
1 Do chronically stressed rats show a decreased sweet consumption when none or short periods of fasting are used instead?

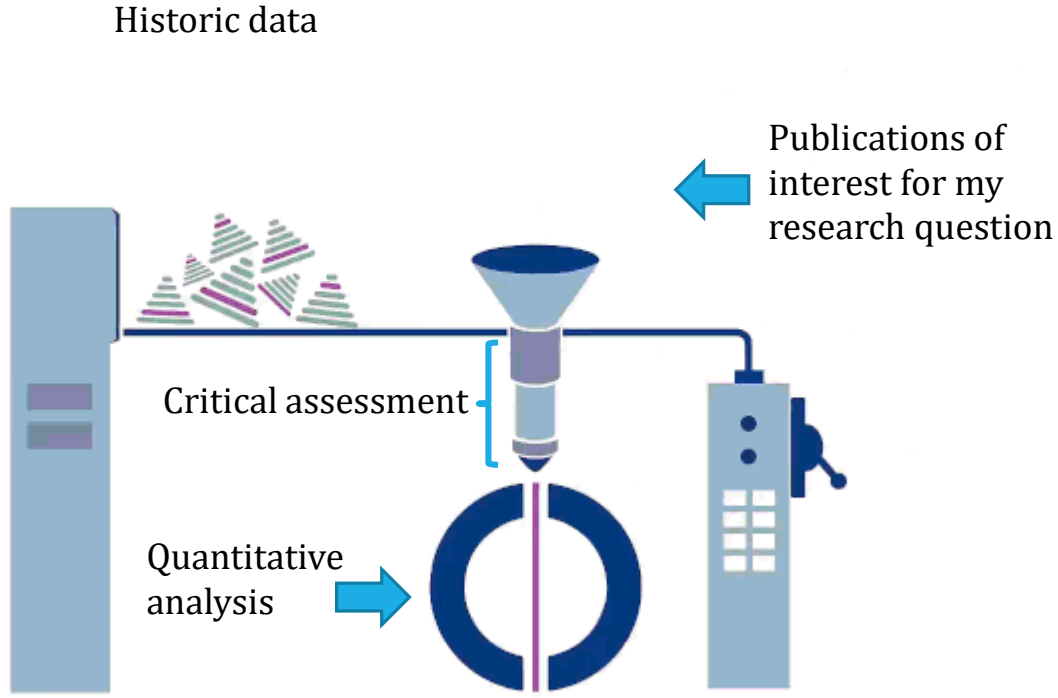
ICSS

HEDONIC DRIVE

2 Do chronically stressed rats show an increased stimulation threshold?

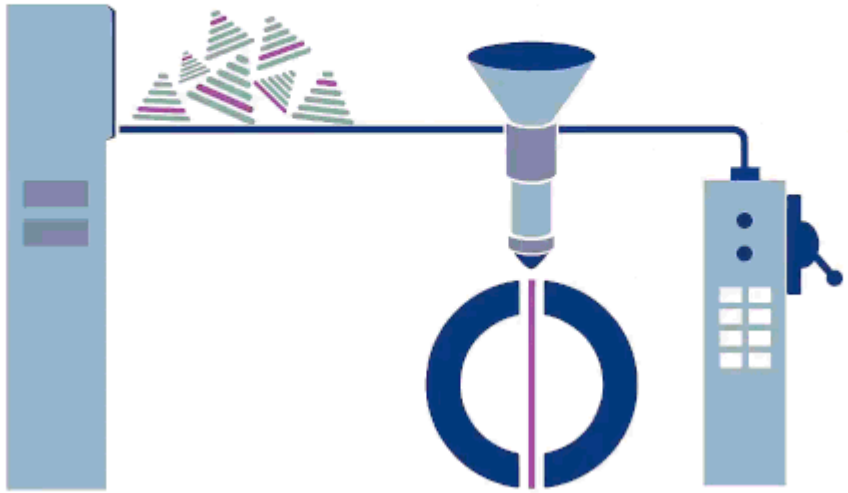
SYSTEMATIC REVIEWS AND META-ANALYSIS





Images sources: https://r1learning.com/blog/2020/02/upon-what-evidence-are-evidence-based-practices-based-4pjtt ; https://cccrg.cochrane.org/Infographics

SYSTEMATIC REVIEWS AND META-ANALYSIS



Available data

Replacement

Reduction

Reconcile conflicting data

Assess quality of the evidence

Refinement

Images sources: https://r1learning.com/blog/2020/02/upon-what-evidence-are-evidence-based-practices-based-4pjtt ; https://cccrg.cochrane.org/Infographics

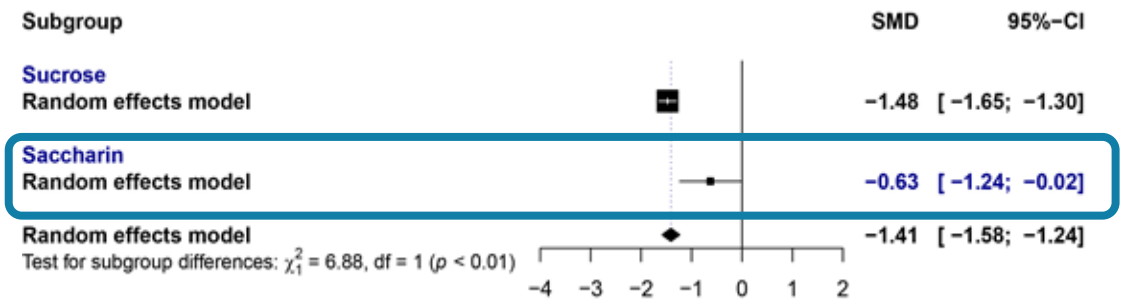
1

Do chronically stressed rats show a decreased sweet consumption when none or short periods of fasting are used instead?

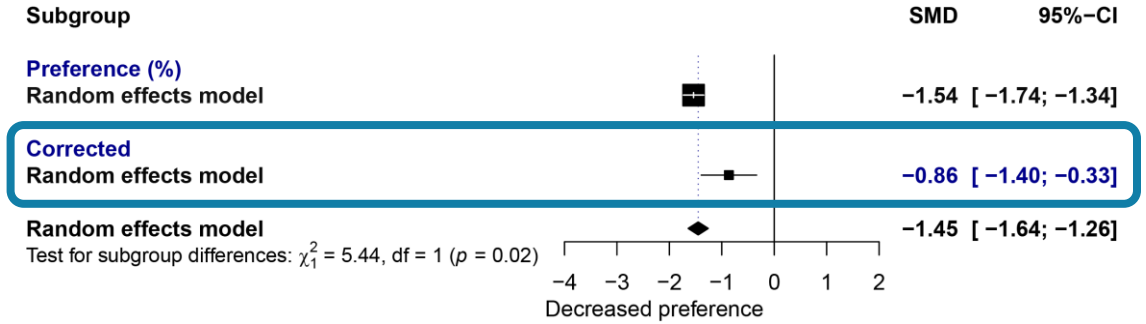
YES, BUT!

Berrio et al. 2023a

Non caloric solution



Correction for body weight



EFFECT SIGNIFICANTLY REDUCED

1

Do chronically stressed rats show a decreased sweet consumption when none or short periods of fasting are used instead?

YES, BUT!

EFFECT SIGNIFICANTLY REDUCED

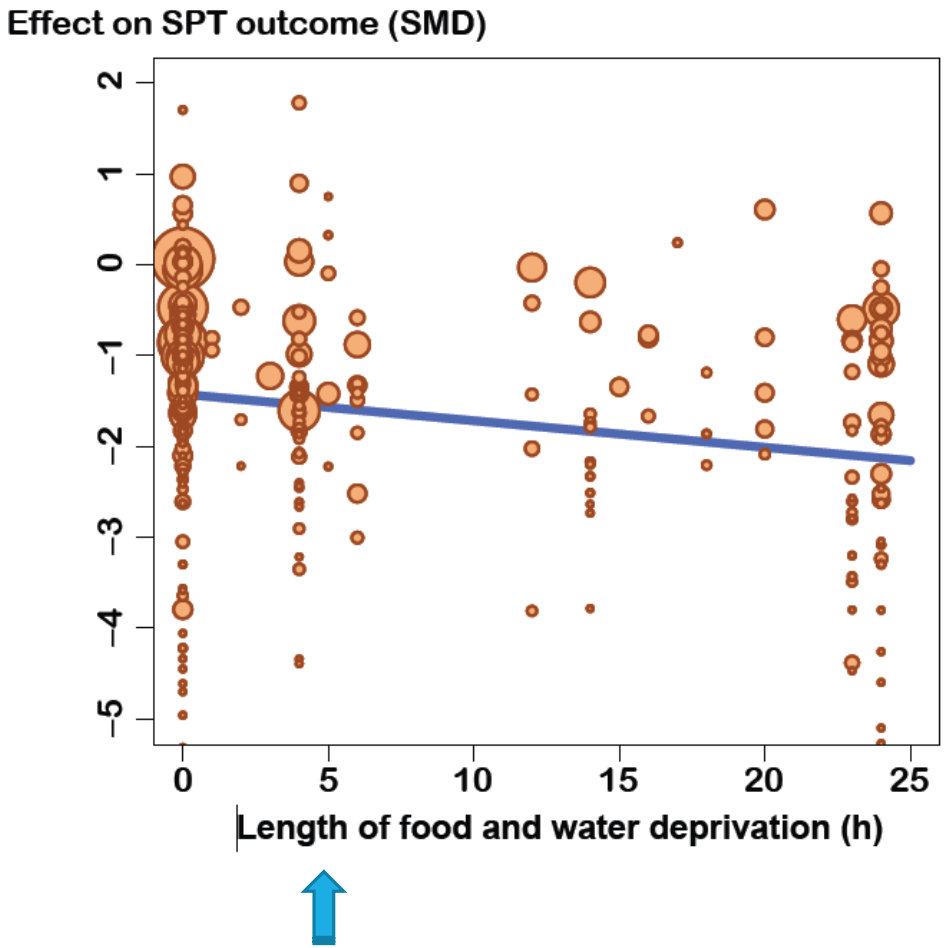
Non caloric solution

Correction for body weight

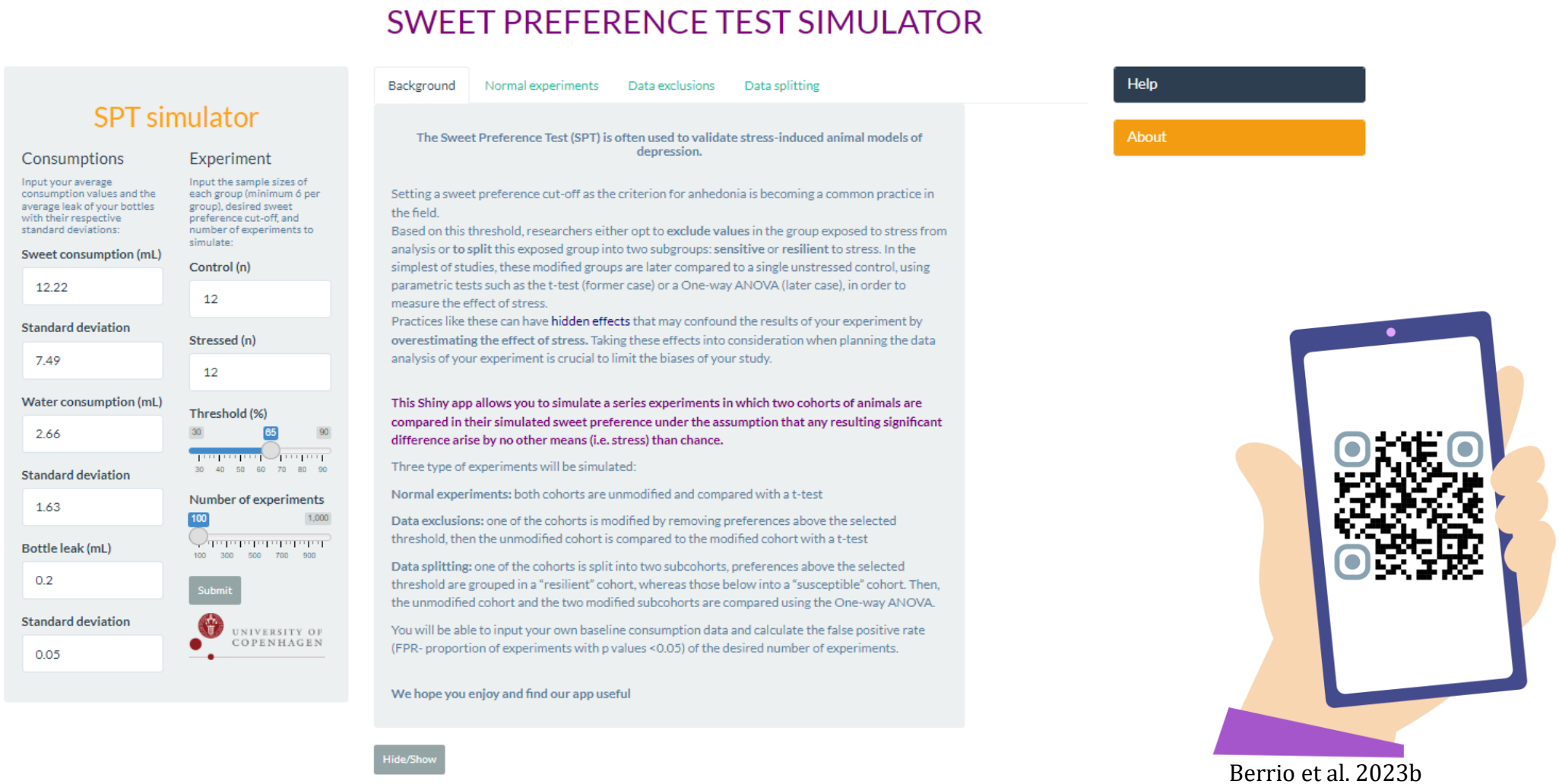
&

LONGER PERIODS OF FASTING CONFOUNDS EFFECT

Not reliable



Cut-off for susceptibility and resilience?



Berrio et al. 2023b

http://jenb.shinyapps.io/App-1

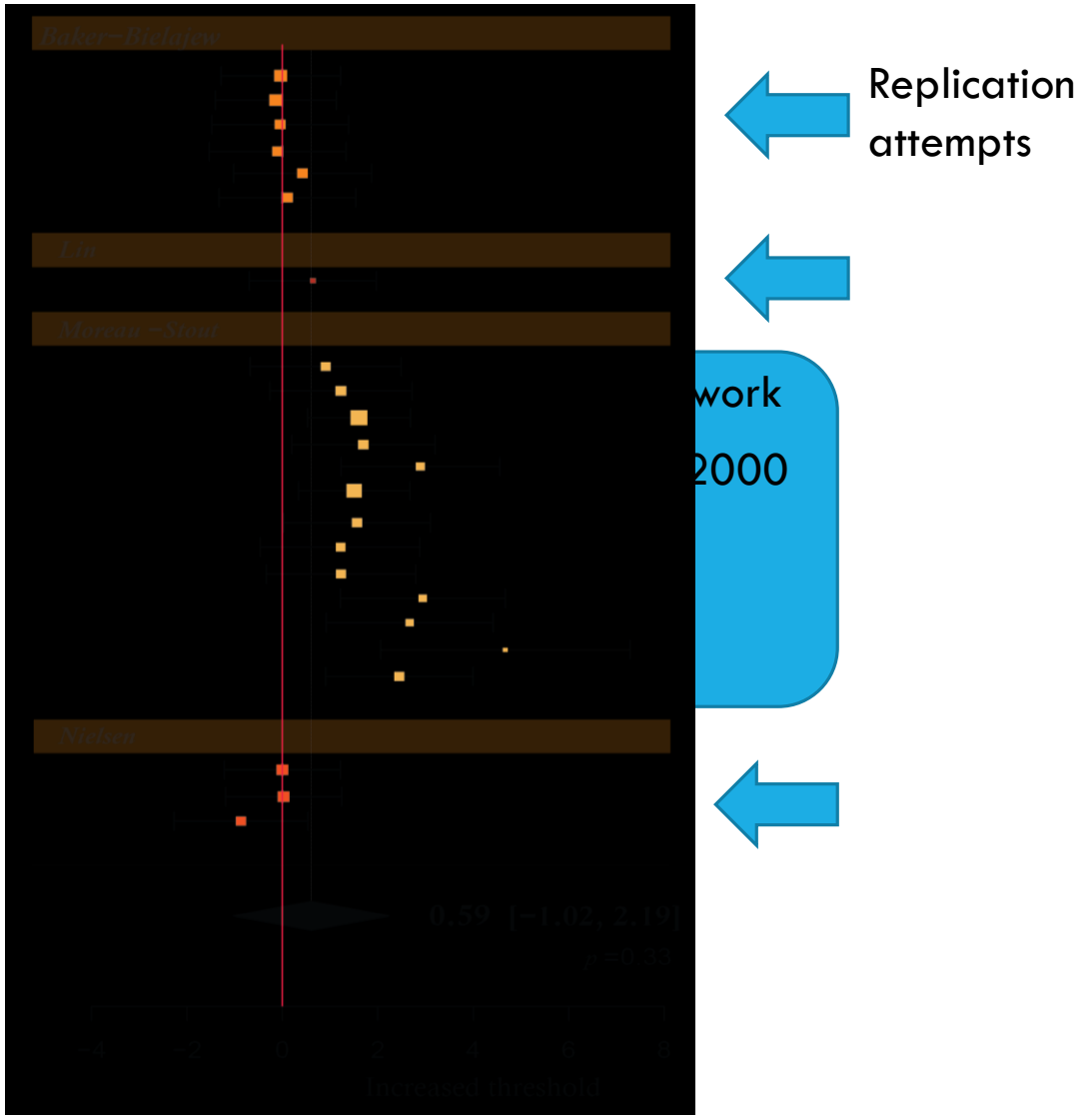
2

Do chronically stressed rats show an increased stimulation threshold and is it correlated with sweet consumption?

NO

LACK OF REPLICATION OF INITIAL RESULTS

Specific factors not identified



Conclusions

- ✓**Depriving the animals of food and water is not necessary nor advised (Test Refinement)**
- ✓Even without long deprivations, a **metabolic component** seem to underlie the effect. Needs to be controlled for **(Test & Model Refinement)**
- ✓Reliability of the **SPT** is still questioned
- ✓No evidence in support that the model is associated with a change in self-stimulating behavior
- ✓Reliability of the **model** for stress–induced anhedonia?

Anhedonia =

SPT	ICSS
DECREASED SWEET CONSUMPTION	INCREASED STIMULATION THRESHOLD
?	X


MARTY, WE'VE GOT TO GO BACK...
BACK THROUGH OUR OLD LEADS!

Thank you

Danmarks 3R-Center

RRR

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Bf3R

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