The effects of relaxin-3 knock down neurons on body weight and food intake in female rats

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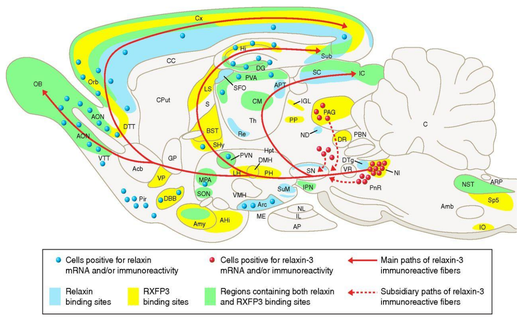
Introduction

Eating Disorders

According to Diagnostic and Statistical Manual of Mental Disorders, DSM-5, eating disorders affect up to three times more women than men[1,2].

The first signs appear during early adolescence[3].

THE RELAXIN-3 (RLN3) is an orexigenic neuropeptide which is mainly produced in the nucleus incertus (NI), in the brain[4].



Bathgate et al. 2013

RLN3 is implicated in several mechanisms such as:

INCREASE

FOOD INTAKE
McGowan et al. 2005

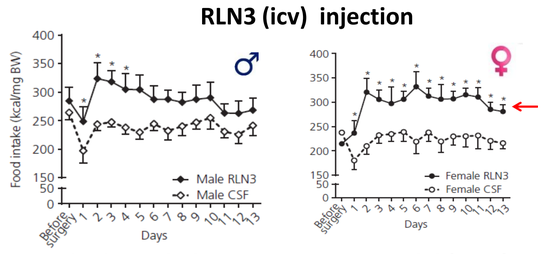
MOTIVATION FOR PALATABLE FOOD
Smith et al. 2014

STRESS RESPONSE
Watanabe et al. 2011

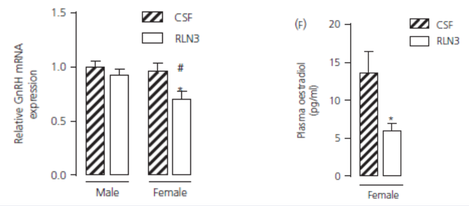
DECREASE

ANXIETY-LIKE BEHAVIOR
Ryan et al. 2013

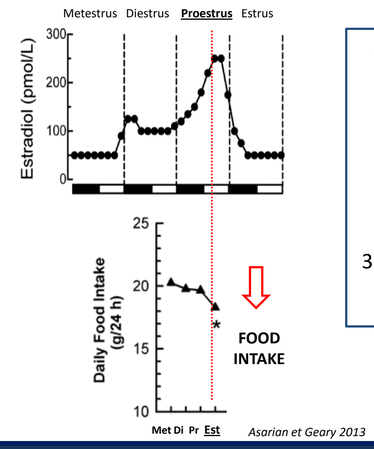
Chronic Intracerebroventricular RLN3 (icv) injection



The hypothalamic pituitary gonadal (HPG) axis



Estradiol effect on food intake during the estrous cycle in rats



Asarian et Geary 2013

SUMMARY

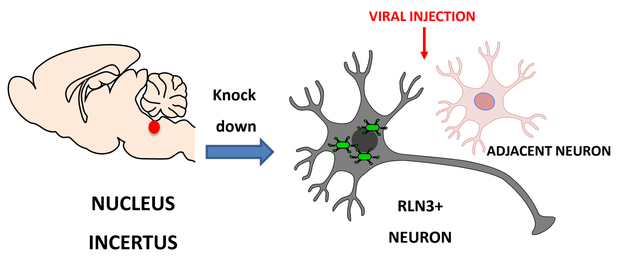
1. Eating disorders affect **mostly women.**
2. **RLN3** presents an orexigenic effect which **is stronger in female** rats.
3. RLN3 affects the **HPG axis in female** rats.

OBJECTIVE: To study the effect of silencing RLN3 neurons in the Nucleus Incertus, in female rats, on food intake (FI), body weight (BW) and anxiety-like behavior.

Methods

Sprague Dawley Rats
226-250g (PND 50)
Individually housed
n = 19

MicroRNA (miRNA) infection via adeno associated virus (AAV) vector into the nucleus incertus.



GROUPS

1. **Knock down (KD):** miRNA against RLN3. n=10.
2. **Control:** miRNA control. n=9.

PROCEDURE

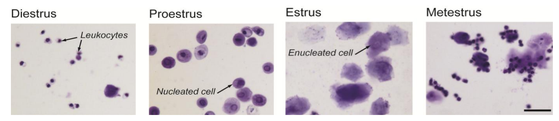
WEEK	1	1-3
TREATMENT	SURGERY	VIRUS INFECTION

WEEK	4- 6	7	8
TREATMENT	BW - FI	ANXIETY TEST	SACRIFICE

During diestrus or metestrus phases

Estrous cycle

Characterization of vaginal cytology:



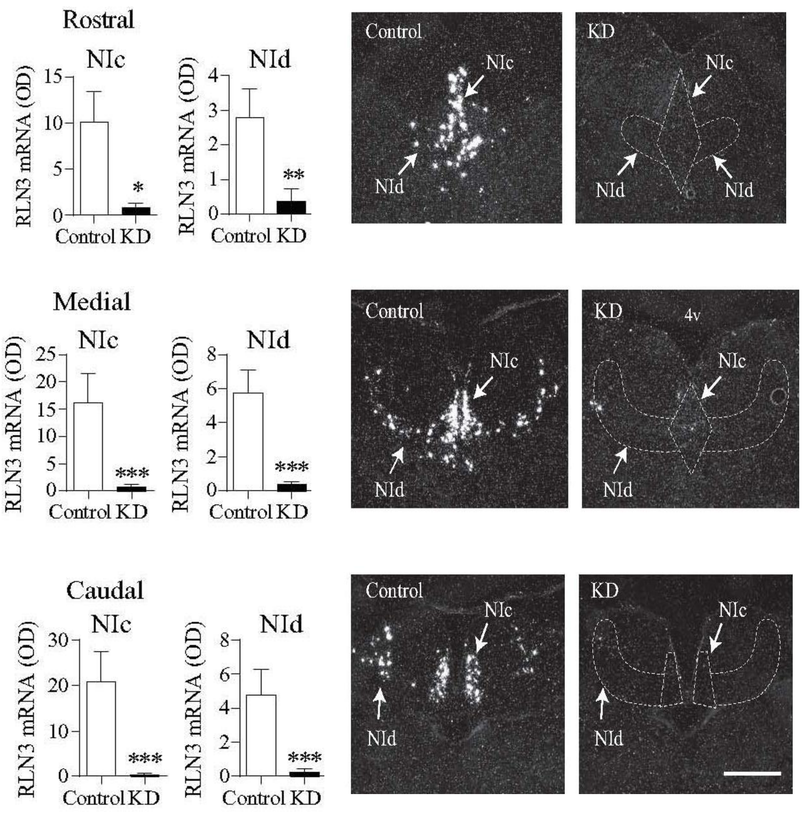
Assays

In situ hybridization (ISH)

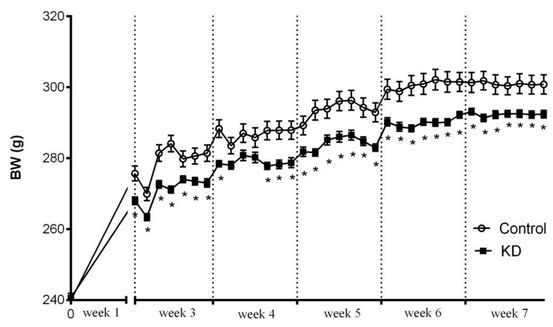
ELISA

Results

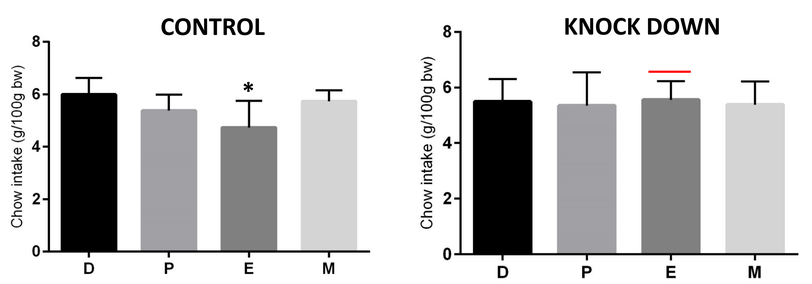
VALIDATION OF THE KNOCK DOWN IN THE NUCLEUS INCERTUS



DECREASE ON BODY WEIGHT

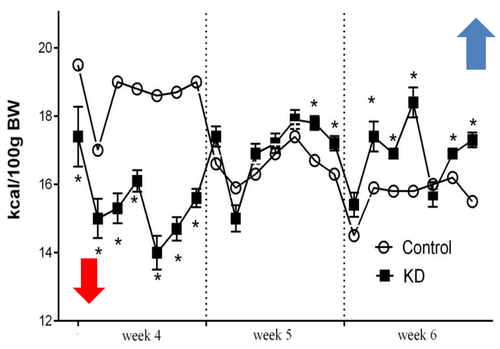


IMBALANCE ON FOOD INTAKE DURING ESTROUS PHASE

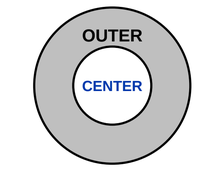


D: diestrus,
P: proestrus,
E: estrus,
M: metestrus

IMBALANCE ON FOOD INTAKE



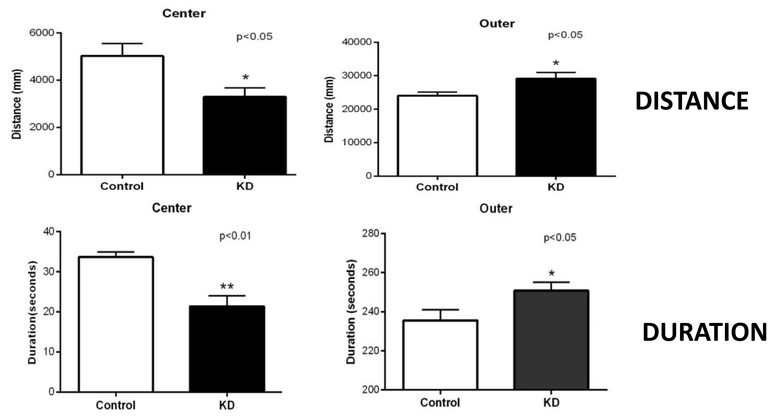
INCREASE IN ANXIETY-LIKE BEHAVIOUR



ANXIETY-LIKE BEHAVIOR

Avoidance of bright areas

Exploration Locomotion



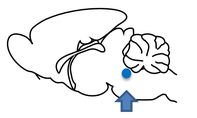
DISTANCE

DURATION

Conclusion

Sprague-Dawley during early adulthood

Knock down of RLN3 $^{+}$ neurons



NUCLEUS INCERTUS

Body weight

Food intake

Food intake during estrus cycle

Anxiety-like behavior

Knock down of RLN3 expression in the NI of female rats induced loss of body weight, disturbance on food intake during estrous cycle and higher anxiety-like behavior compared to control rats. Further experiments (ISH) will be carried out to address the central and peripheral mechanisms underlying the behaviors studied.

References: [1]Black, D.W. and J.E. Grant, *DSM-5® Guidebook: The Essential Companion to the Diagnostic and Statistical Manual of Mental Disorders*. 2014: American Psychiatric Pub; [2]*Diagnostic and statistical manual of mental disorders (DSM-5®)*. Fifth edition ed. 2013: American Psychiatric Pub; [3]Bulik, C.M., *Eating disorders in adolescents and young adults.* Child and adolescent psychiatric clinics of North America, 2002. **11**(2): p. 201-218; [4]Bathgate, R., et al., *Relaxin family peptides and their receptors.* Physiological reviews, 2013. **93**(1): p. 405-480.