Impairments in sensorimotor gating and working memory.

Del Río C (1),Oliveras I (1),Blázquez G (1), Cañete T (1), Tobeña A (1), Fernández-Teruel A (1).
(1)Dept. Psychiatry & Forensic Medicine, Institute of Neuroscience, Autonomous University of Barcelona, Bellaterra, Spain.

INTRODUCTION

The *Roman* high– and low-avoidance (RHA and RLA) rat strains, have been bidirectionally selected and bred for their very good (RHA) or extremely poor (RLA) ability to acquire the two-way active avoidance task in a shuttle-box.

Main features:

Anxiety/fear and stress susceptibility **(RLA > RHA)** attention **(RLA > RHA)** impulsivity traits **(RLA < RHA)** novelty-/drug-seeking behavior **(RLA < RHA)** chronic psychostimulant-induced locomotor and dopamine sensitization **(RLA < RHA)**.

RHA-I also shows **↑ of 5-HT2A** receptors while they are **devoid of mGluR2** expression in **prefrontal cortex and hippocampus**,

We also included the **NIH/Hs** heterogeneus rat stock because it might be a useful tool as a control group, considering their genetic profile.

Valid animal models are needed in the study of Schizophrenia (SCZ).

OBJECTIVE

Exp.1: Evaluate Roman rat strains in Prepulse inhibition (PPI) for information processing at post natal day (PND) 30, 50 and 100.

Exp.2: Evaluate Roman rat strains and Heterogeneus rats (NIH/Hs) in PPI at PND 100 and in Morris Water Maze (MWM) for "working memory" at PND120

MATERIAL & METHODS

All rats were male

Exp.1: Prepulse Inhibition (PND 30,50,100)

PND30: RLA / RHA (n=9)

PND50-100 : RLA n= 26 / RHA n= 19

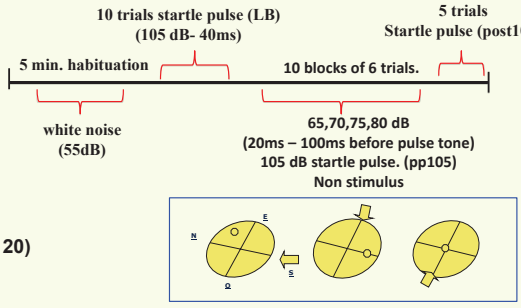
Exp 2: Prepulse Inhibition (PND 100)

RLA n= 36 / RHA n= 41 / NIH/Hs n= 30

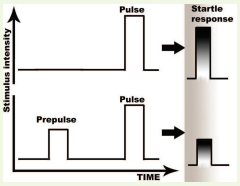
Morris Water Maze

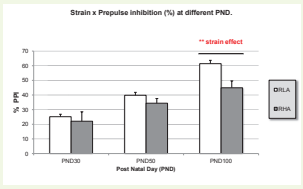
"Delayed matching –to- place task (PND120)

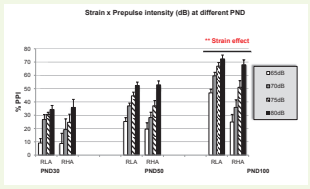
RLA n= 19 / RHA n= 16 / Hs n= 33

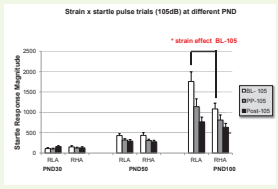


Exp 1. PREPULSE INHIBITION (PPI) AT POST NATAL DAY (PND) 30, 50 AND 100.





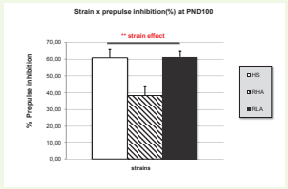


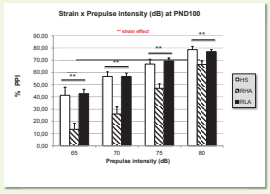


High percentage of PPI = High efficiency of sensorigating abilities

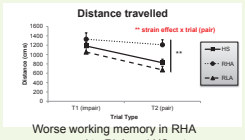
Exp.2 Prepulse inhibition (PPI) at PND 100 between RLA/RHA and NIH/Hs

Delayed matching –to- place task (MWM)

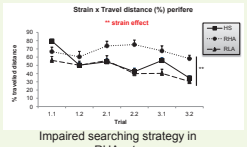




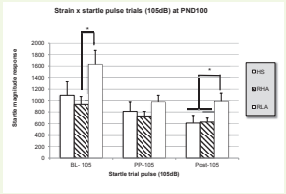
Working memory refers to the imrpovment of the second trial (pair) compared to the first one (impair).

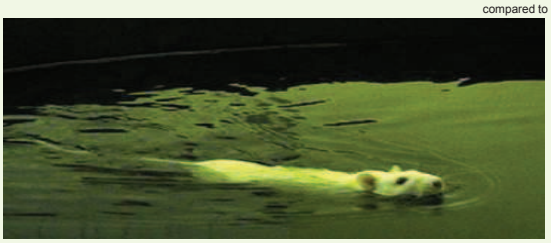


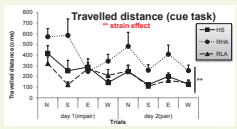
Worse working memory in RHA compared to RLA and HS rats



Impaired searching strategy in RHA rats







RHA rats are impaired in Cued learning

Cue task

Platform was 1 cm above the water, marked with a visible flag (intramaze cue). 2 trial days, starting from each cardinal point

CONCLUSIONS

EXP.1

✓No differences in PPI between male RHA-I and RLA-I rats at 30 (puberty) and 50 (adolescence) days of age, with significant differences –i.e. better PPI in RLA-I than in RHA-I rats- appearing when rats are 100 days old.

✓This resembles the typical course of schizophrenia, which commonly shows its onset in the early adulthood.

EXP.2

✓Confirm the differences between Roman rat strains in processing information at PND100 (lower PPI in RHA compared to RLA).

✓RHA shows impairments in working memory compared to RLA (Delayed matching –to-place task), and in the cue task. NIH/Hs

✓PPI levels from heterogeneus NIH-HS rats fall between RHA and RLA scores in PPI and in the Morris Water Maze (MWM)

VALID ANIMAL MODEL IN SCHIZOPHRENIA

HIPERACTIVIDAD DOPAMINÉRGICA

IMPULSIVIDAD

RHA > RLA

Hasta el momento el único modelo conocido knock-out espontáneo del receptor mGluR2, y sobre-expresión del 5-HT2A

DEFICITS FILTRAJE ATENCIONAL (PPI)

DÉFICITS FUNCIONES EJECUTIVAS (WM)

PATRÓN NEUROQUÍMICO 5-HT2A/mGluR2

REFERENCES

1. Oddo S *et al.* (2003) *Neurone* 39: 409-21; *Neurobiol Aging* 24: 1063-70. 2. Oddo S *et al.* (2006) *J Biol Chem* 281: 1599-604. 3. Billings LM *et al.* (2005) *Neuron* 45: 675-88. 4. Fernández-Teruel A *et.al.* (2002) *Pharmachol Biochem Behav* 73: 233-45. 5. Giménez-Llort *et al.* (2007) *Neurosci Biobehav Rev* 31: 125-47. 6. Arendash GW *et al.* (2004) *Neuroreport* 15: 1751-4.

ACKNOWLEDGEMENTS

Special thanks to J.Beauquis and L.Manzo for the histology studies and brain pictures. In accordance with 86/609/EEC regarding care and use of animals for experimental procedures. Supported by 'RamonCajal Program', 2005SGR 00885, EME2005-140267, EME2006-140335, SAF2006-13642 and Swedish Alzheimer's Foundations. http://antalya.uab.es/dpsiquiatia/en/grupRecerca_1.php