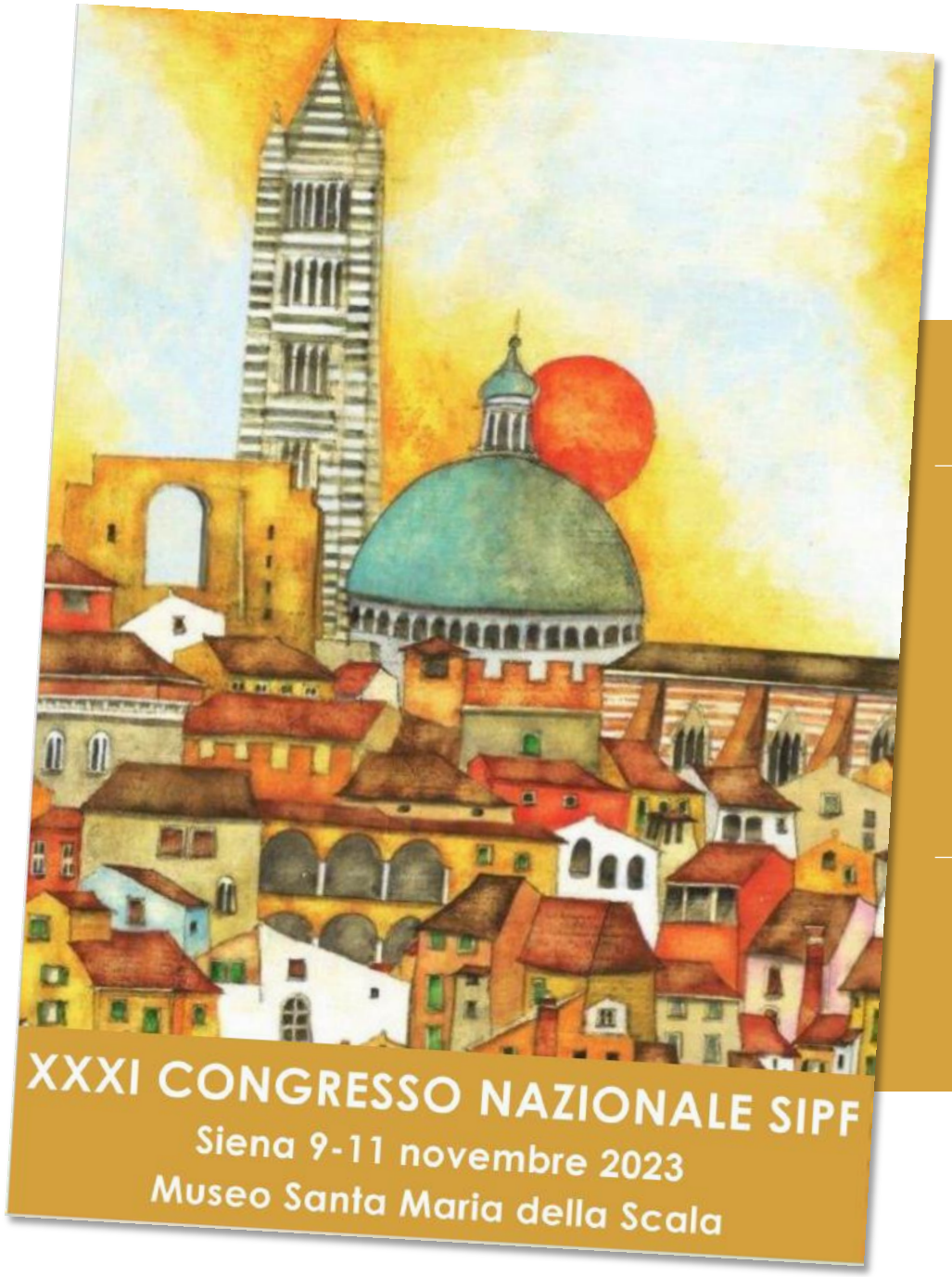


KEYNOTE LECTURE I

Multidimensional Translational Behavioral Neuroscience in Aging and Alzheimer's Disease

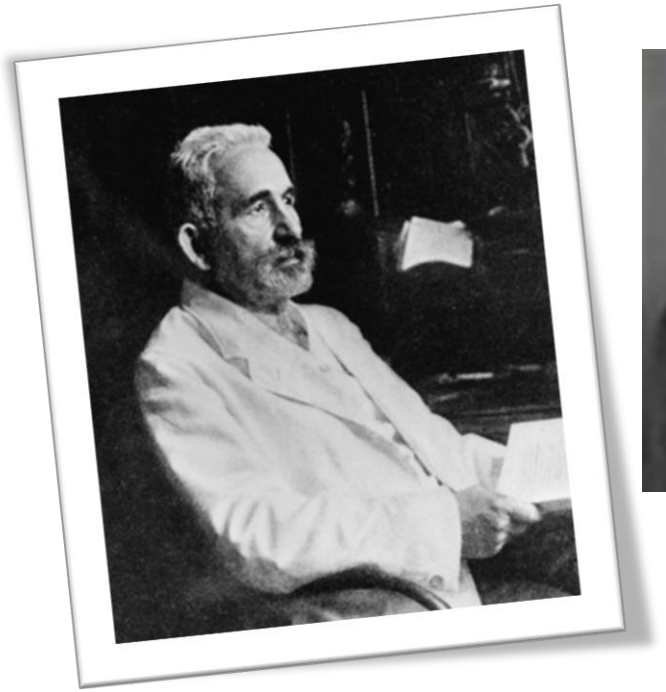
Lydia Giménez-Llort

Siena 9 novembre 2023

UAB
Universitat Autònoma de Barcelona

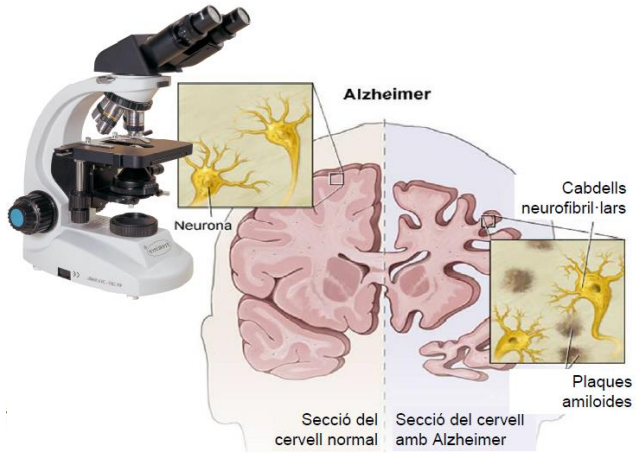
Departament de Psiquiatria i Medicina Legal UAB

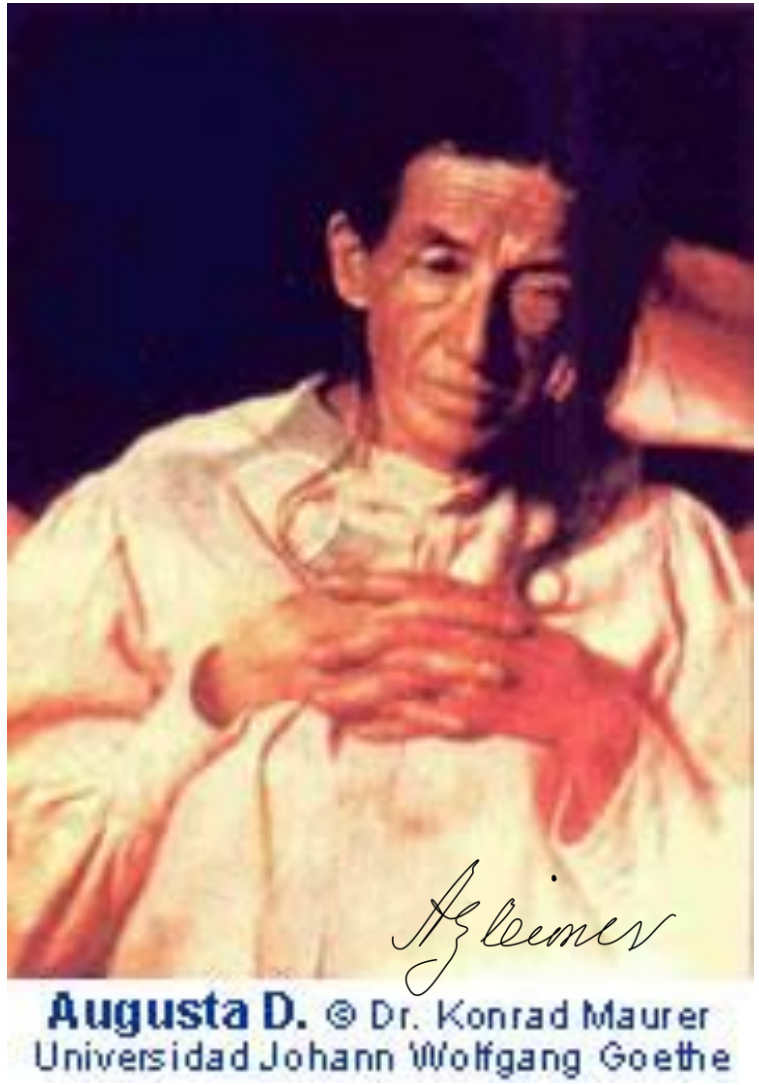
INc Institut de Neurociències



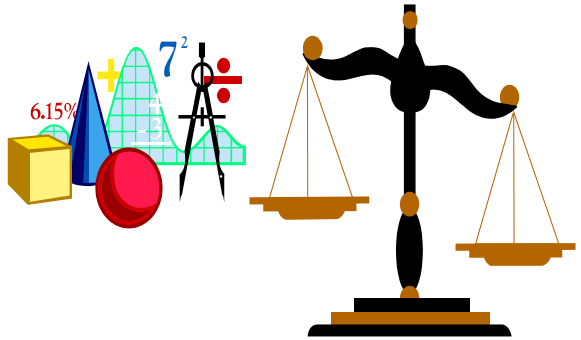
Dr. Emil Kraepelin

Dr. Alois Alzheimer





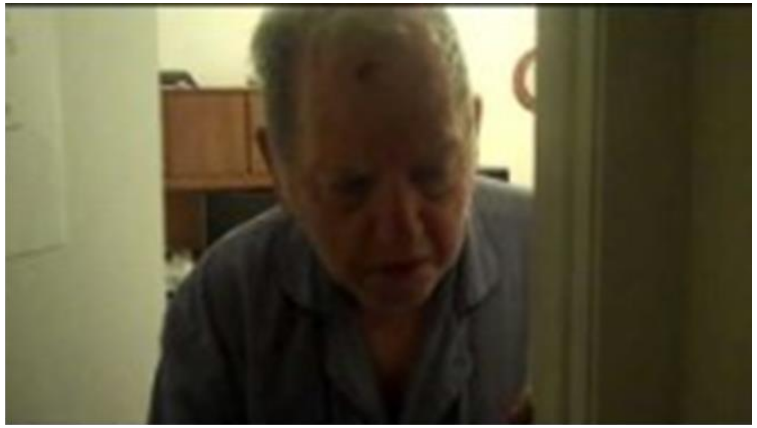
The other patient
A complex clinical history



Living with Deme

Dementia

1. Memory
2. Abstract thinking
3. Judgement
4. High cognitive functions



Alzheimer's Sundown Syndrome – awake all night
by howard251a https://youtu.be/9Ak1tgzv_0Q
Min 0.14 to 1:42, 5:40 to end

BPSD Behavioral and Psychological sympthoms of dementia

Agitation, aggressive, psychosis, anxiety

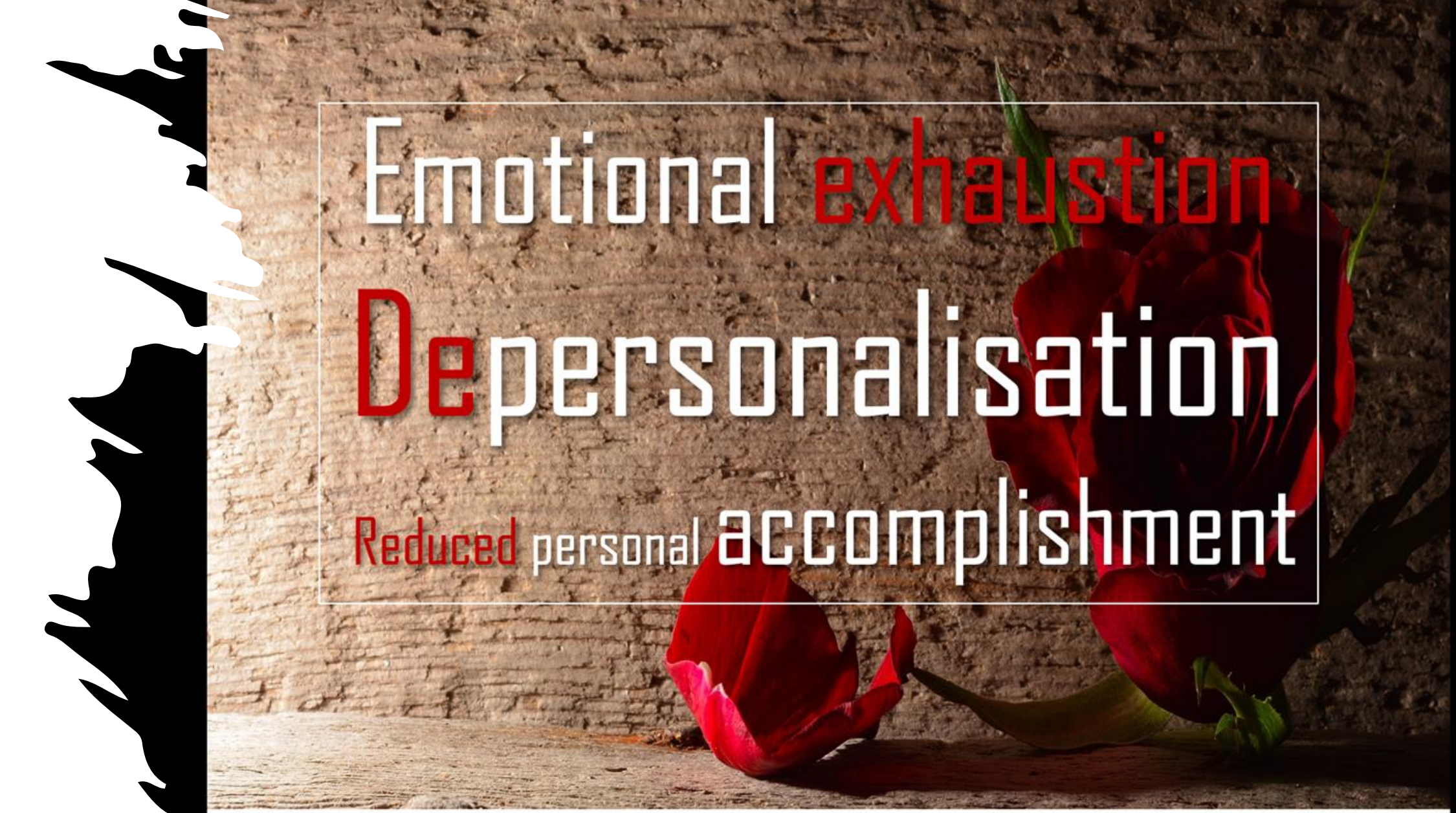
Apathy

5-15% AD + major depression

20-40% AD + illusions and hallucinations

Sundowning behavior

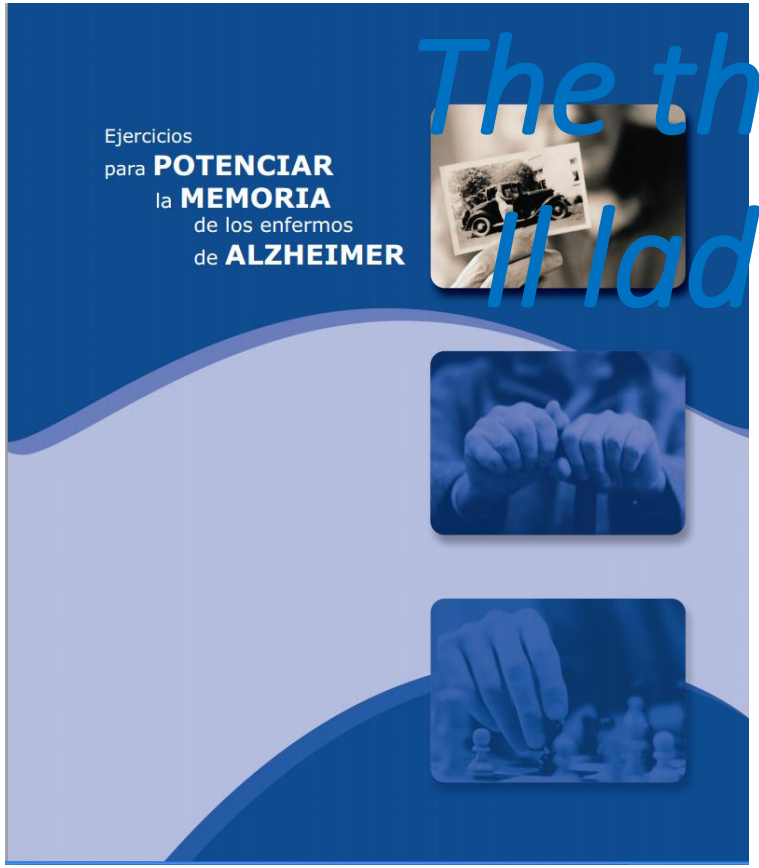
"Living with dementia" https://youtu.be/loksPQ7Q8tM
by Social Care Institute for Excellence
http://www.scie.org.uk/



CuidaDORA 10 maneres de cuidar als què cuiden – Lydia Giménez-Llort – Institut de Neurociències, UAB
Scientific Corner, Microxerrades Científiques -28 de Setembre 2018 - CosmoCaixa Nit de la Recerca a Catalunya

The thief of memory

Il ladro di memoria



Nuestro objetivo

Queremos animar a todo aquel que lo necesite a que utilice este manual de ayuda. Lo más importante es conseguir que las capacidades cognitivas se preserven durante el mayor tiempo posible, enlentecer el curso rápido de la enfermedad, y potenciar la relación del enfermo con su medio, intentando hacer mas fácil y llevadero el largo camino que supone el padecer algún tipo de demencia.

Pedro Gil, Raquel Yubero, Llanos Morón.
Unidad de Memoria. Servicio de Geriatría
Hospital Universitario San Carlos (Madrid)

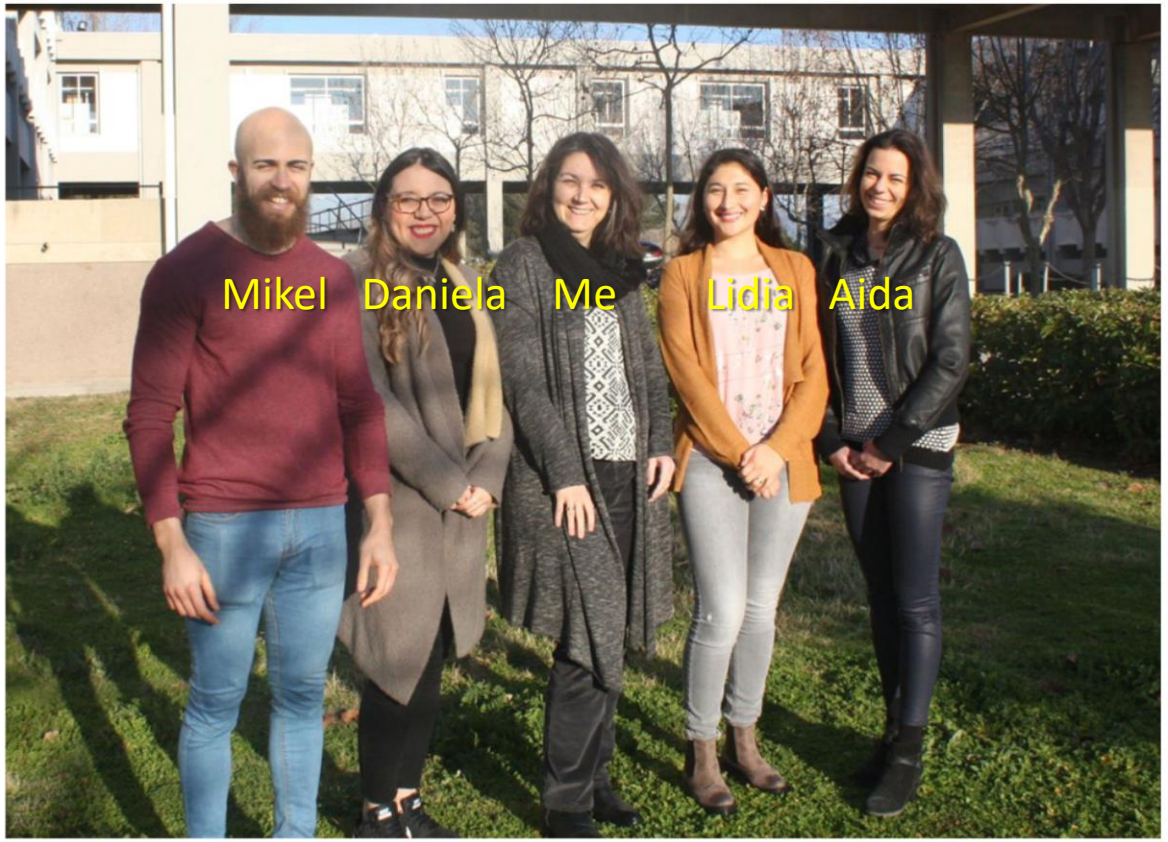
Indice

The Umbrella effect

Giménez-Llort, 2014

PSYCHOGERIATRIC MULTIDIMENTIONAL DINAMIC EVALUATION

CLINICAL	FUNCTIONAL	MENTAL	SOCIAL
biomedical, biopsicosocial	daily life activities	neurocognitive , BPSD	family, caregivers,others



Translational Behavioral Neuroscience Group

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ScienceDirect

Journals & Books

Register

Sign in

Translational Medicine

Translational medicine defined by the term “from bench to beside” refers to the transfer of results or new knowledge achieved in the laboratory toward health innovation.

From: Substance Use and Addiction Research, 2023

Related terms:

Neoplasm, Combination Therapy, Clinical Trial, Therapeutic Procedure, Translational Research, Tissues, Stem Cell, Biological Marker, Malignant Neoplasm, Chemotherapeutic Agent

View all Topics >

« from the experimental platform to the hospital bed »
Science, 1992

« transformation medicine »
Lancet, 1995

New York, June 19-July 22, 1946

World Health Organization

International Health Conference, 1946

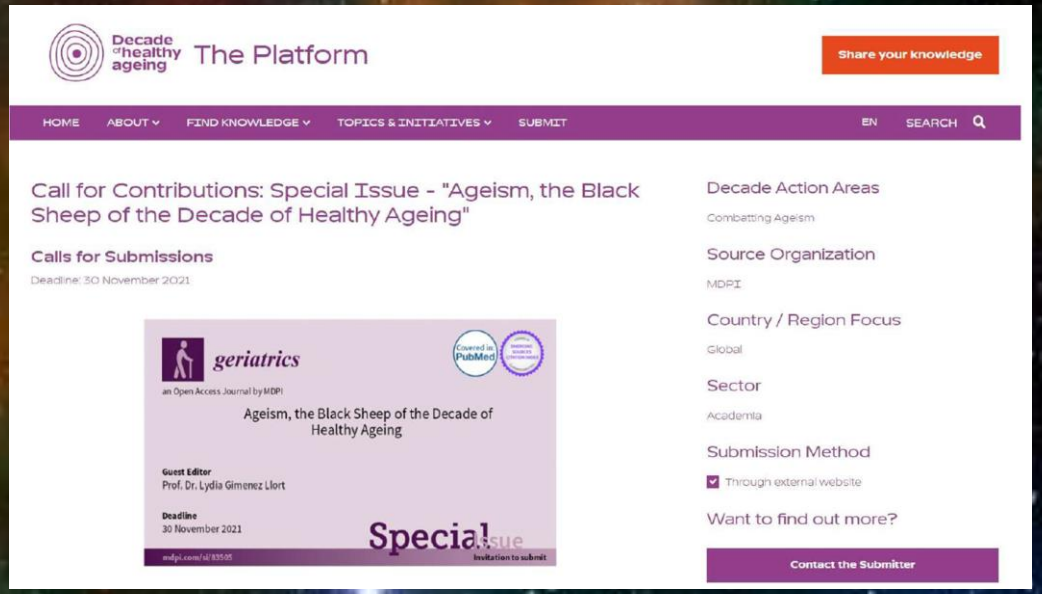
HEALTH "State of complete physical, mental and social Well-being and not only the absence of **conditions or diseases"**

in NEGATIVE TERMS / pathogenesis

Gender Medicine

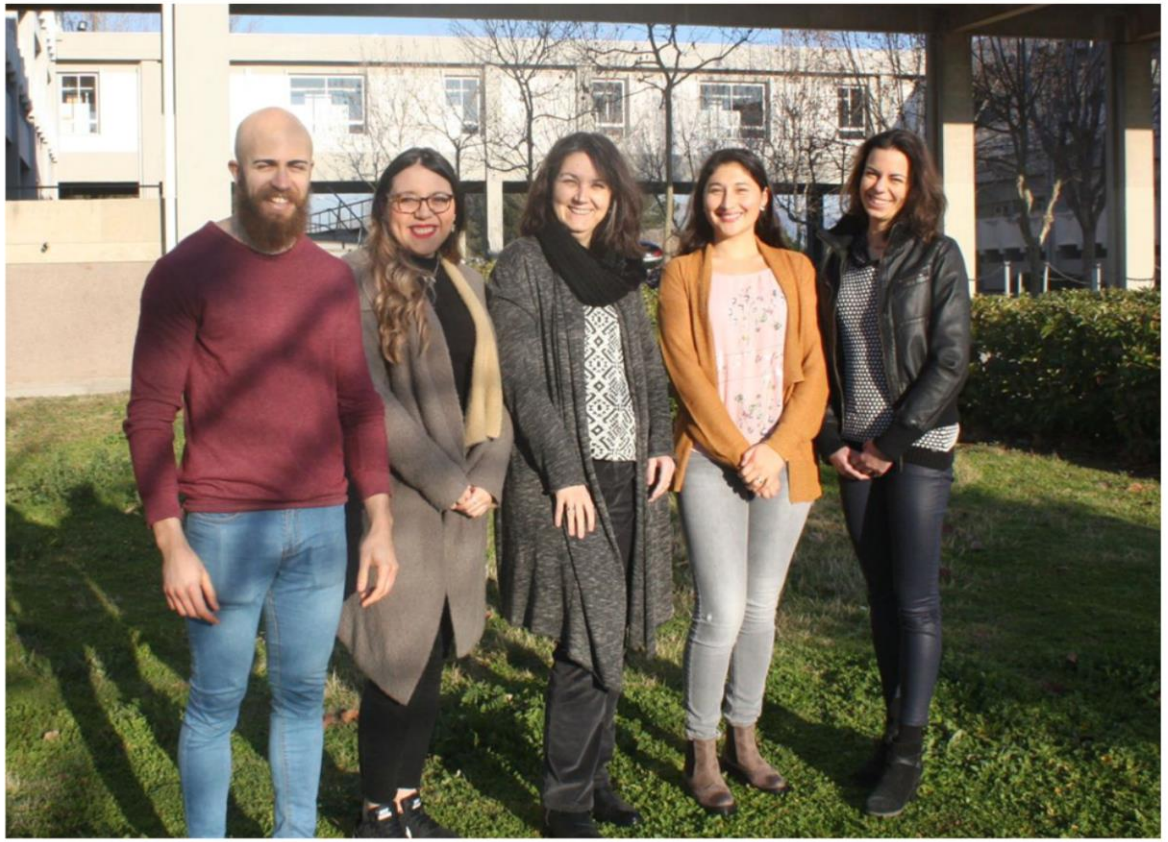
The Medicine of the Third Millennium

Gender Medicine: a task for the third millennium
Baggio, Giovanella *et al. Clin Chem Lab Med*, 2013, 51:713-27



Decade of Healthy Aging

(2020-2030)



Translational Behavioral Neuroscience Group

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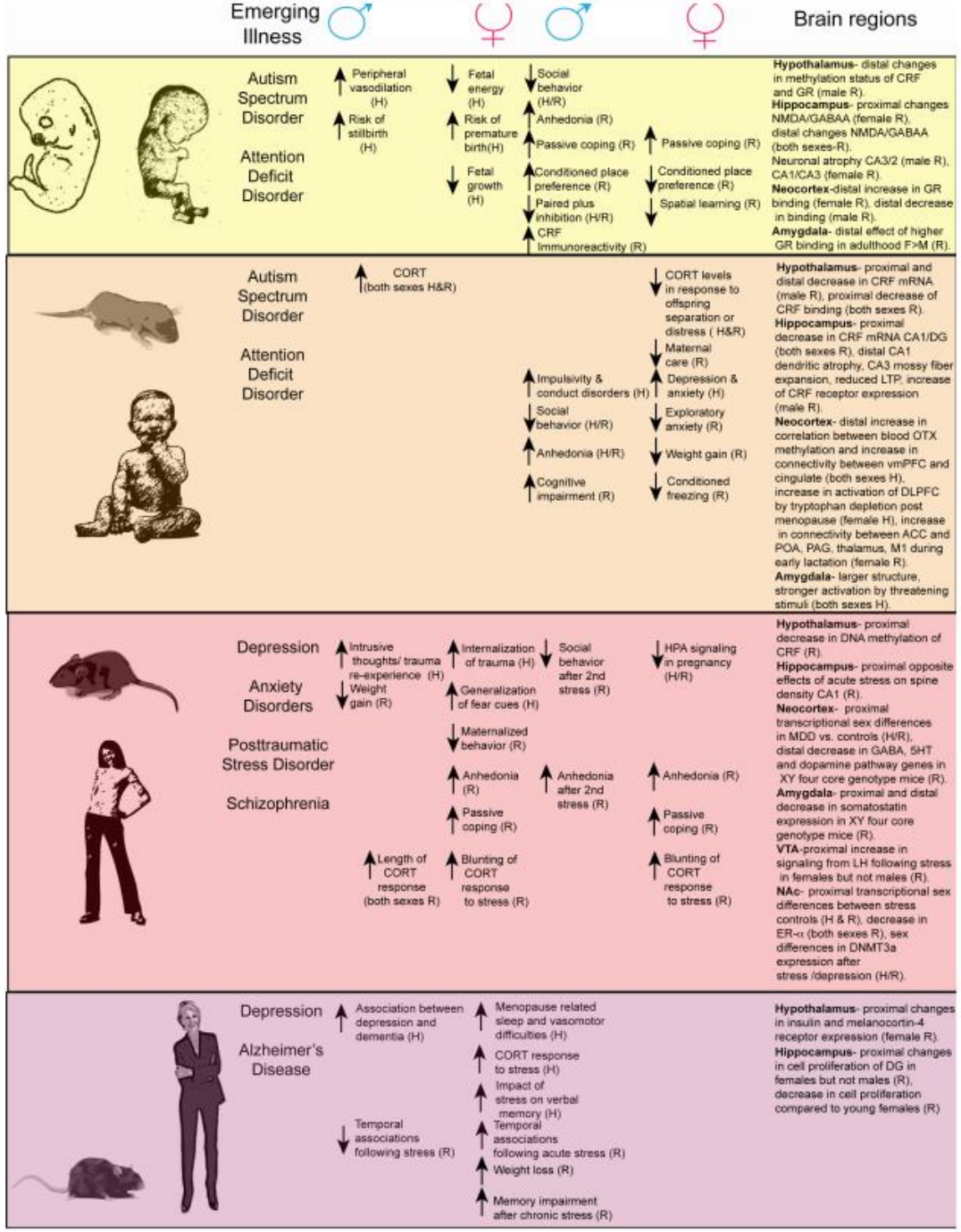
Departament de Psiquiatria i Medicina Legal UAB

INc Institut de Neurociències

- Cycle of life · Function and dysf(x) · Onset /monitoring/ EoL
- Comprehensive behavioral phenotype characterization
- Validation of models of disease
- Behavioral tools: Rethinking/ Refinement/ Repurposing
- Pre-clinical proof-of-concept / screening

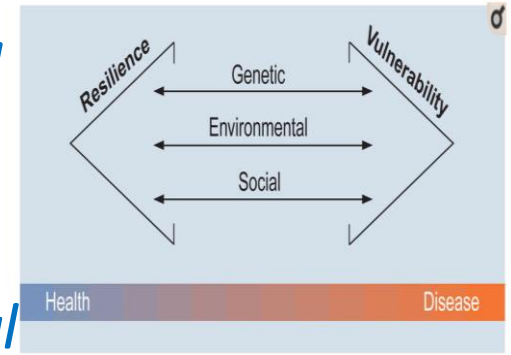


Life cycle age/aging

Intergenerational

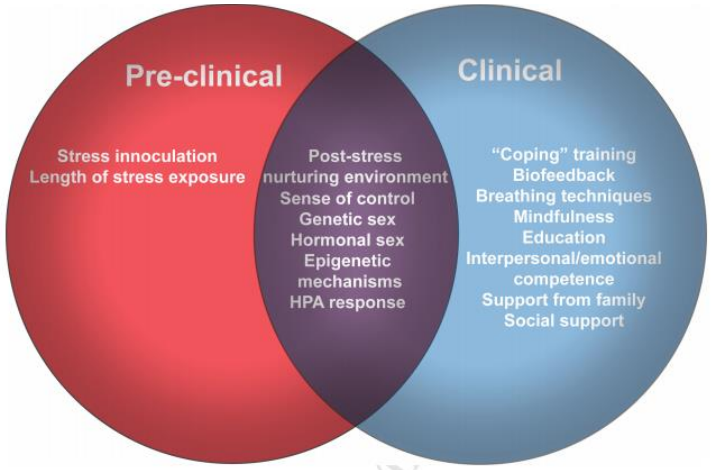
Continuum

Longitudinal vs transversal

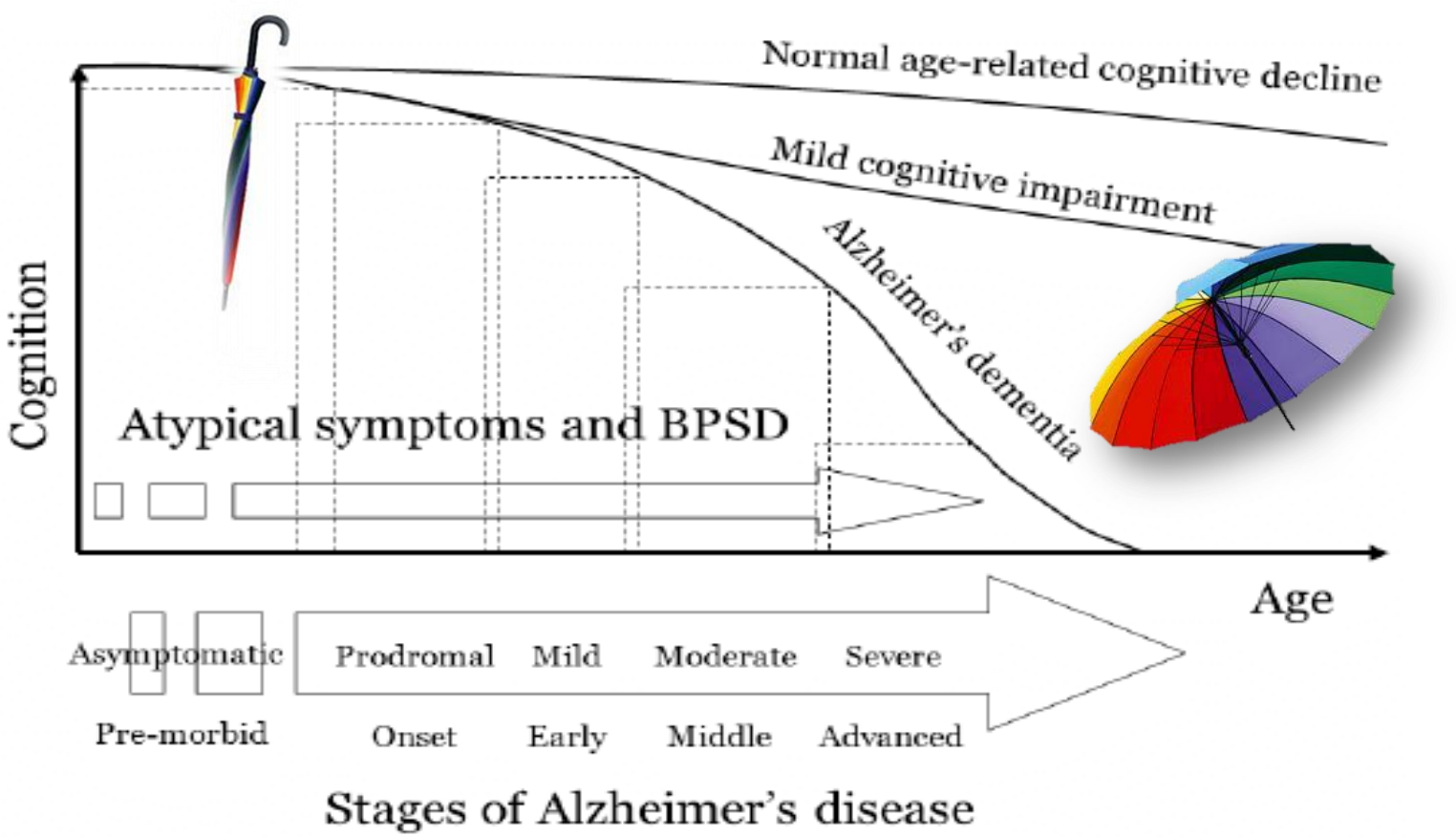


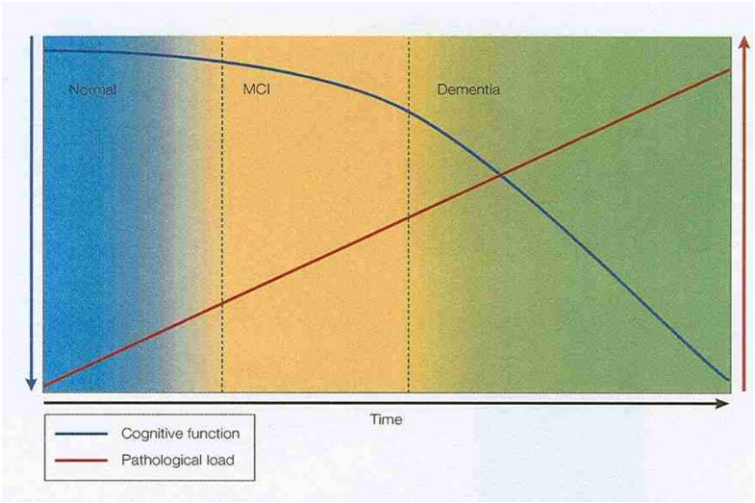
The forces of vulnerability and resilience can push an individual towards disease or health

Vulnerability and resilience involve genetic, environmental and social forces.



Premorbid, Prodromal





4 Scuola de la Differenza

IN RELAZIONE: PERCHE'?
BIOETICA, BIOPOLITICA E TANATOPOLITICA,
XIII EDIZ. SCUOLA ESTIVA DELLA DIFFERENZA 2015
Marisa Forcina, Usalento

Giochi e contatto fisico nei topi con Alzheimer
Lydia Giménez-Llort

3 False NEGATIVE

2 Dose/ Effectivity RESPONSE

1 Windows of OBSERVATION

How diseases

differ

between men and women
in terms of

Prevention

clinical signs,

therapeutic

approach

prognosis,

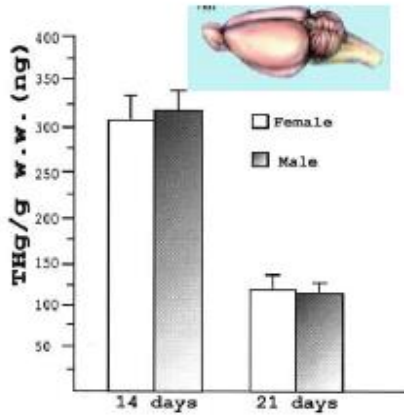
psychological and social

impact

LG2018

Karolinska Institutet

Environmental hazards
Psychiatric and neurological disorders



ELSEVIER

Environmental Toxicology and Pharmacology 00 (2000) 000–000

ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY
ETAP

www.elsevier.com/locate/etap

Prenatal exposure to methylmercury changes dopamine-modulated motor activity during early ontogeny: age and gender-dependent effects

L. Giménez-Llort [a], E. Ahlbom [b], E. Daré [b], M. Vahter [c], S.-O. Ögren [a], S. Ceccatelli [b,*]

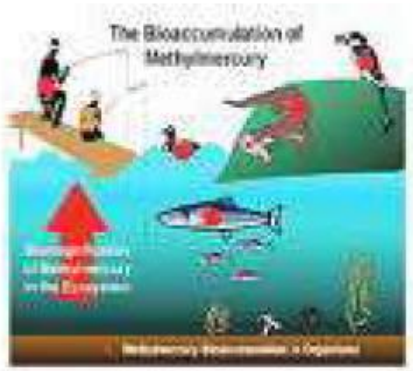
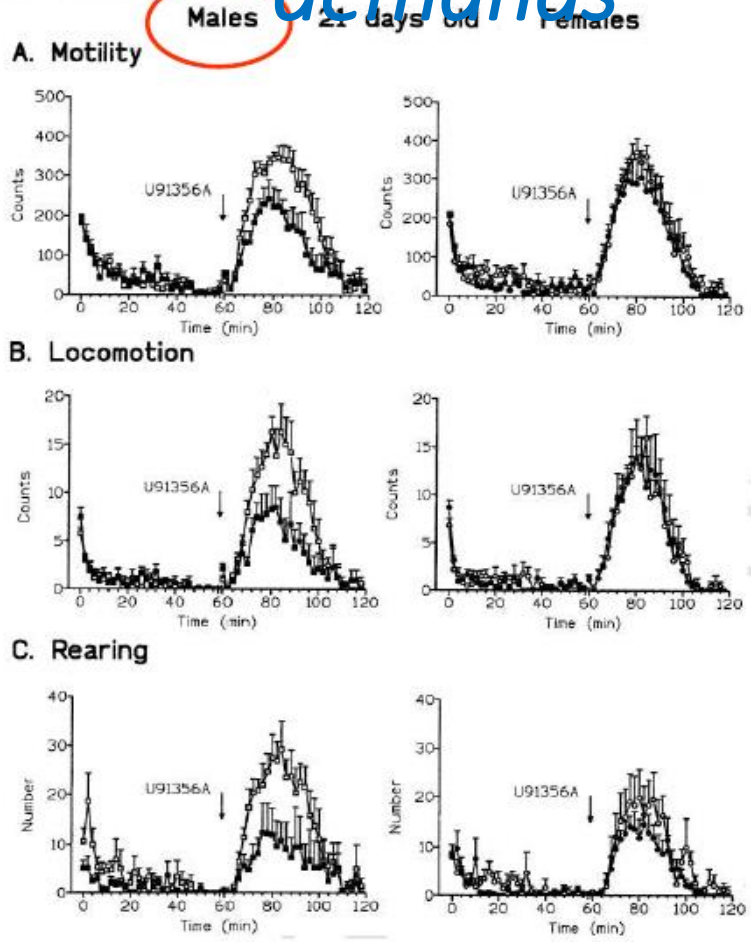


Table 1
Effect of MeHg exposure on body weight (g) of animals at PND14 and 21[a]

	Control	Treated
PND 14		
Male	34.22 ± 1.72	33.92 ± 1.12
Female	33.10 ± 1.70	33.20 ± 1.07
PND 21		
Male	54.10 ± 2.69	50.78 ± 2.40
Female	52.35 ± 2.47	52.17 ± 2.29

[a] Values are expressed as mean ± S.E.M.

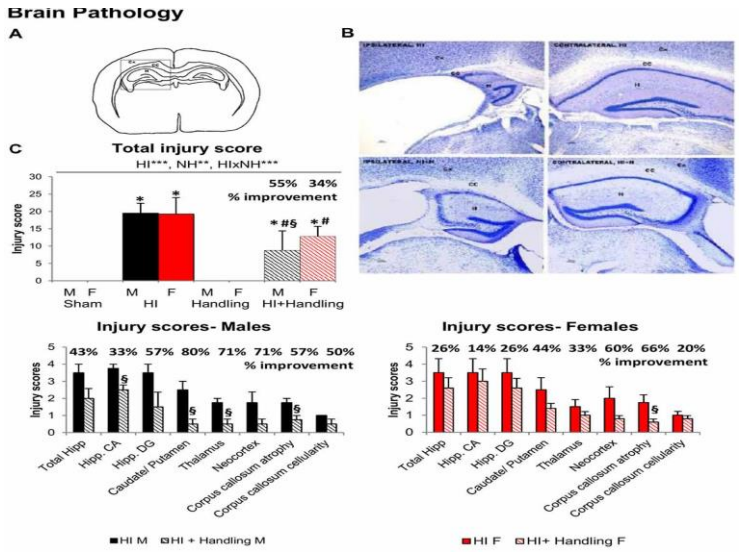
Windows Task demands



ORIGINAL RESEARCH ARTICLE
Front. Behav. Neurosci., 13 February 2019 | https://doi.org/10.3389/fnbeh.2019.00007

Severe Perinatal Hypoxic-Ischemic Brain Injury Induces Long-Term Sensorimotor Deficits, Anxiety-Like Behaviors and Cognitive Impairment in a Sex-, Age- and Task-Selective Manner in C57BL/6 Mice but Can Be Modulated by Neonatal Handling

Aida Muntsant[1,2], Kalpana Shrivastava[2,3], Mireia Recasens[2,3] and Lydia Giménez-Llort[1,2]*
[1]Department of Psychiatry and Forensic Medicine, School of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain
[2]Institut de Neurociències, Universitat Autònoma de Barcelona, Barcelona, Spain
[3]Department of Cell Biology, Physiology & Immunology, Universitat Autònoma de Barcelona, Barcelona, Spain



frontiers in Behavioral Neuroscience

Multidimentional

BEHAVIORAL DOMAINS	BEHAVIORAL TESTS	Sex effect				Age effect	Handling effect
		Male PND23	Male PND70	Female PND23	Female PND70		
SENSORIMOTOR							
Reflexes	Reflex test		✓		✓	✓	✓
Equilibrium	Wire rod test			✓		✓	
Prehensility	Hanger test	✓				✓	
Paw preference	Cylinder test	✓		✓			✓
LOCOMOTOR							
Locomotor activity	Motor activity test	✓				✓	✓
Vertical activity	Open field		✓			✓	✓
NEUROPSHYCHIATRIC- LIKE							
Anxiety	Open field, Dark-light		✓				✓
Neophobia	Corner test		✓				✓
Emotionality	T-maze				✓		
COGNITIVE							
Working memory	T-maze						
Memory	Morris water maze		✓		✓		✓
Acquisition tasks	Morris water maze		✓		✓		✓

PER ESSERE RAGAZZA

THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Biological Sciences
cite as: J Gerontol A Biol Sci Med Sci, 2018, Vol. 73, No. 9, 1147–1157
doi:10.1093/gerona/gly031
Advance Access publication 19 February 2018

OXFORD

Original Article

Sexual Dimorphism in the Behavioral Responses and the Immunoendocrine Status in d-Galactose-Induced Aging

Raquel Baeta-Corral, PhD,[1,2] Rafael Castro-Fuentes, PhD,[3] and Lydia Giménez-Llort, PhD[1,2]

[1]Translational Behavioral Neuroscience Group, Institute of Neuroscience and [2]Department of Psychiatry and Forensic Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain. [3]Department of Basic Medical Sciences, School of Health Sciences, Section Medicine, University of La Laguna, Tenerife, Spain.

D-gal monosaccharide abundant milk products, fruits, vegetals
Chronic systemic D-gal – Accelerated aging – ROS AGEproducts

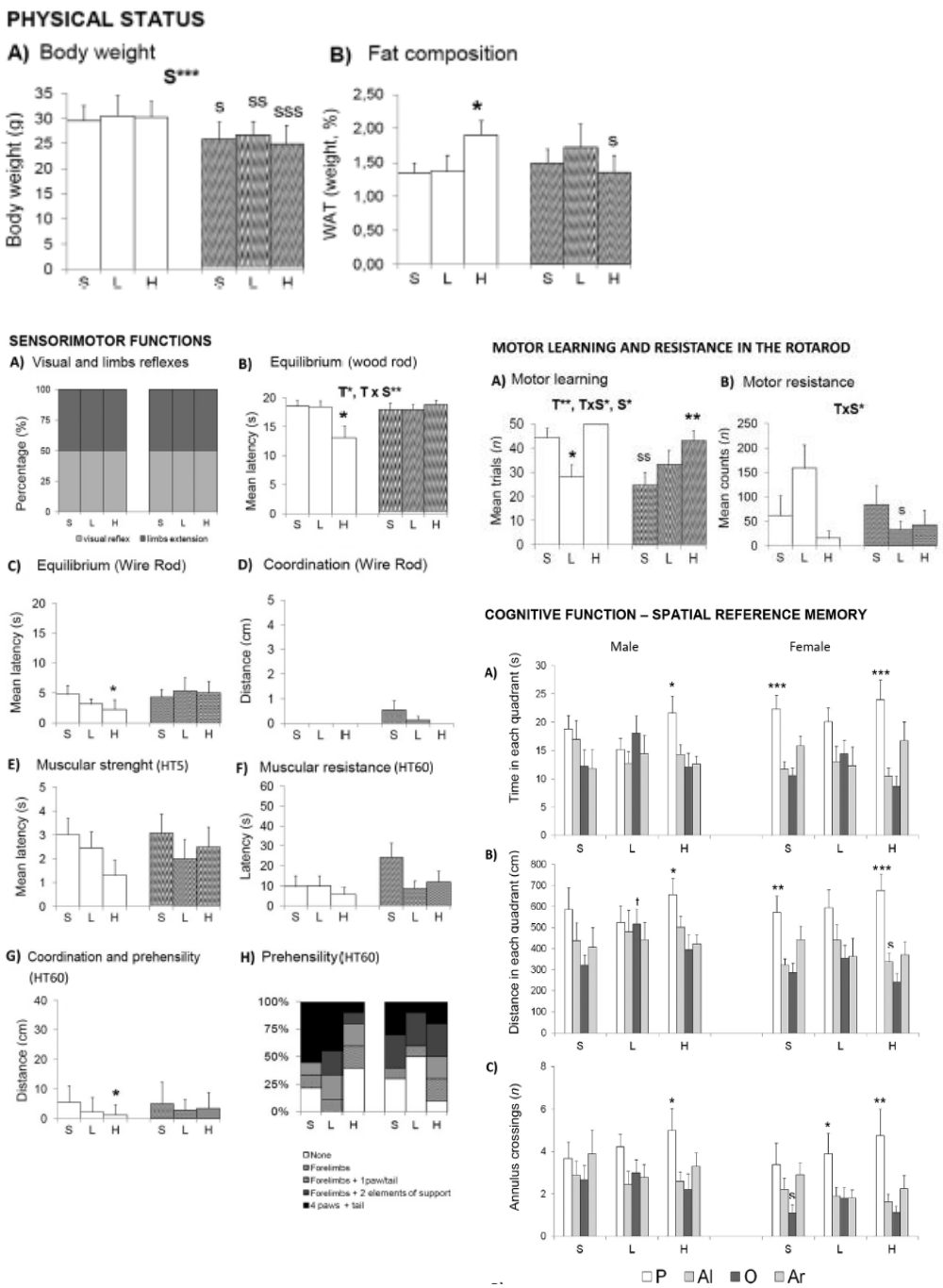
Comprehensive & multifunctional behavioral screening
Convergent validity
L50 H100 mg/kg 58d MF6mo

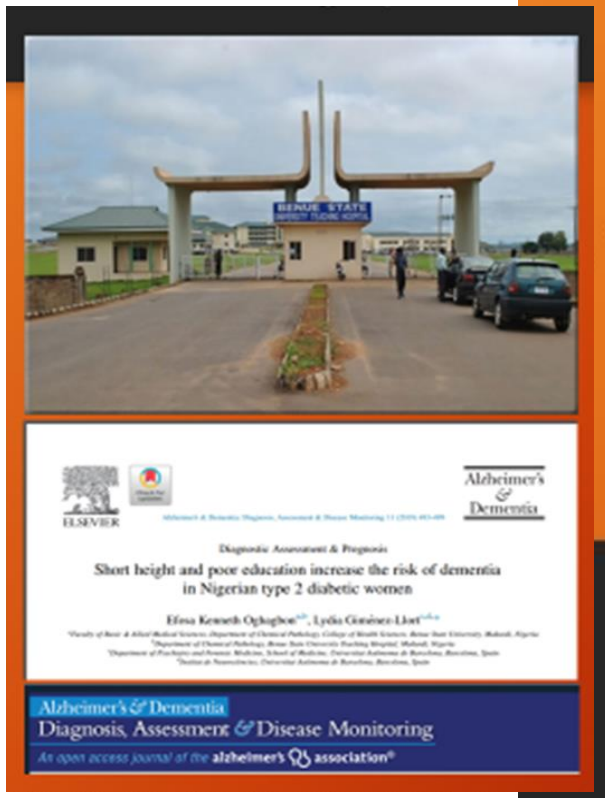
M Sensory impairment
Immunoendocrine senescence
L50 Improved L&M RT, H100 L&M MWM

F dose-dependent worse L (RT), but improved M (MWM)

Different neuronal substrates / functional capacity /
to meet task dependent performance demands

Males and Females can be regarded as two exceptional natural scenarios to study the functional interplay in the crosstalk of homeostatic networks at aging





Sex and Gender-Medicine in Low-to-Middle-Income Countries:

Diabetes-Dementia Storm in sub-Saharan Africa

Lydia Giménez-Llort, José Prieto-Pino
Faeren Dogoh, Monday Ogiator,
Efosa K. Oghagbon

UAB Universitat Autònoma de Barcelona


Heterogeneous
Cognition + BPSD + DLA+ Social
Progressive Neurodegenerative
Pathways Changing
Systems
ADP *vs* ADC

Behavioral Neuroscience

- ✓ Validation (Guideliness)
- ✓ What about normal? Control WT?
- ✓ Test - Screening and validation of the model
- ✓ Face V., Predictive V., Construct V. Convergent V.
- ✓ From unidimentional to Tridimentional: Cognitive + BPSD + DLA and to multidimensional: Motor + Sensorial + Social
- ✓ Translational, Longitudinal
- ✓ Gender dependent

- ✓ Life events + Life style ('Dementia beyond drugs')
- ✓ External interventions (Pharmacol, Immunological, others)

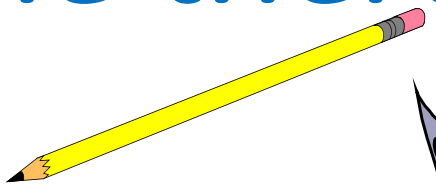
- ✓ Prevention + Therapeutics

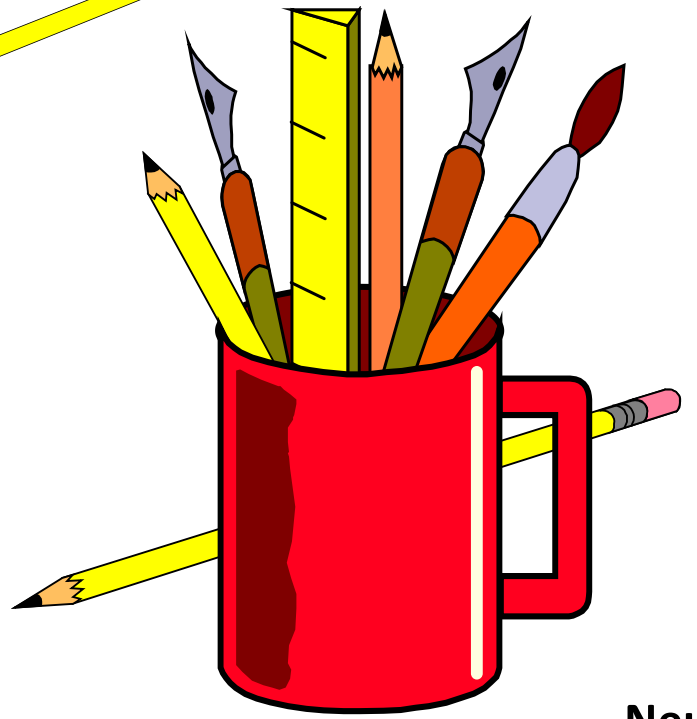
The complexity of the therapeutical strategies

The unique

The best

The exclusive one





Cognition & Memory
Cholinergic deficits

Behavioral Alterations
Neurotransmitters

Neuroprotection & Regeneration
Glutamate antagonists
Genetic Strategies
Growth Factors

Cognitive Dysfunction Syndrome
A Disease of Canine and Feline Brain Aging

Gary M. Landsberg, DVM[a,b,*], Jeff Nichol, DVM[c],
Joseph A. Araujo, BSc[b,d,e]

KEYWORDS

• Cognitive dysfunction syndrome • Brain aging • Behavior • Canine • Feline

KEY POINTS

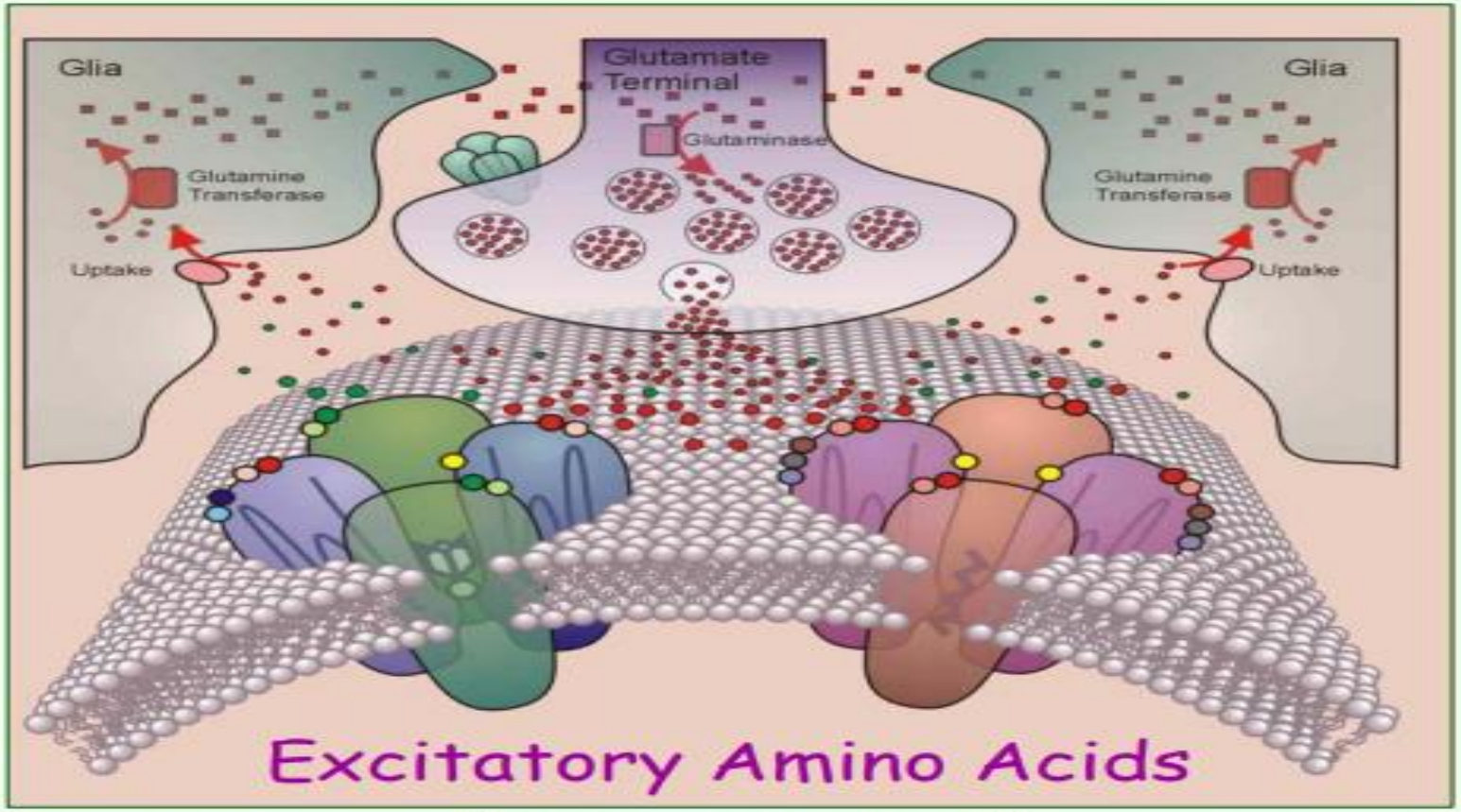
- Brain aging is a degenerative process that for many dogs and cats ultimately progresses to a loss of one or more cognitive domains or impairment of cognitive function.
- Diagnosis of cognitive dysfunction syndrome (CDS) is based on recognition of behavioral signs and exclusion of other medical conditions and drug side effects, which in some cases can mimic or complicate CDS.
- Clinical categories include disorientation, alterations in social interactions, sleep-wake cycles, elimination habits, and activity, as well as increasing anxiety. Deficits in learning and memory have also been well documented.
- Treatment is aimed at slowing the advancement of neuronal damage and cell death and improving clinical signs. Drugs, diet, and supplements can be used alone or concurrently to improve neurotransmission and reduce oxidative damage and inflammation.

Table 1
CDS checklist[1]

Signs: DISHAAL	Age First Noticed	Score 0–3[a]
D: Disorientation/Confusion—Awareness—Spatial orientation		
Gets stuck or cannot get around objects		
Stares blankly at walls or floor		
Decreased recognition of familiar people/pets		
Goes to wrong side of door; walks into door/walls		
Drops food/cannot find		
Decreased response to auditory or visual stimuli		
Increased reactivity to auditory or visual stimuli (barking)		
I: Interactions—Social Relationships		
Decreased interest in petting/avoids contact		
Decreased greeting behavior		
In need of constant contact, overdependent, "clingy"		
Altered relationships other pets—less social/irritable/aggressive		
Altered relationships with people—less social/irritable/aggressive		
S: Sleep–Wake Cycles; Reversed Day/Night Schedule		
Restless sleep/waking at nights		
Increased daytime sleep		
H: Housesoiling (Learning and Memory)		
Indoor elimination at sites previously trained		
Decrease/loss of signaling		
Goes outdoors, then returns indoors and eliminates		
Elimination in crate or sleeping area		
A: Activity—Increased/Repetitive		
Pacing/wanders aimlessly		
Snaps at air/licks air		
Licking owners/household objects		
Increased appetite (eats quicker or more food)		
A: Activity—Apathy/Depressed		
Decreased interest in food/treats		
Decreased exploration/activity/play		
Decreased self-care (hygiene)		
A: Anxiety		
Vocalization, restlessness/agitation		
Anxiety, fear/phobia to auditory or visual stimuli		
Anxiety, fear/phobia of places (surfaces, locations)		
Anxiety/fear of people		
Separation anxiety		
L: Learning and Memory—Work, Tasks, Commands		
Decreased ability to perform learned tasks, commands		
Decreased responsiveness to familiar commands and tricks		
Inability/slow to learn new tasks		

[a] Score: 0 = none; 1 = mild; 2 = moderate; 3 = severe.
Adapted from Landsberg GM, Hunthausen W, Ackerman L. The effects of aging on the behavior of senior pets. Handbook of behavior problems of the dog and cat. 2nd edition. Philadelphia: WB Saunders; 2003. p. 273; with permission.

Animal models for Psychiatric and Neurologic disorders

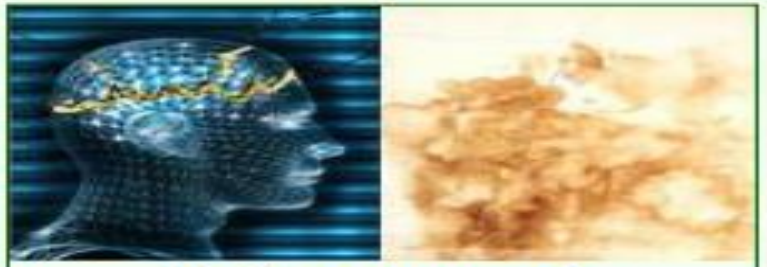


Excitatory Amino Acids

Normal synaptic transmission

Learning & Memory

Developmental plasticity



Epileptogenesis

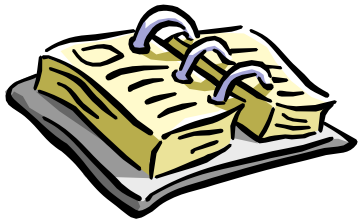
Acute neuropathology

Hypoxia/ischaemia
Stroke
Trauma
Hypoglycaemia
Exogenous toxins

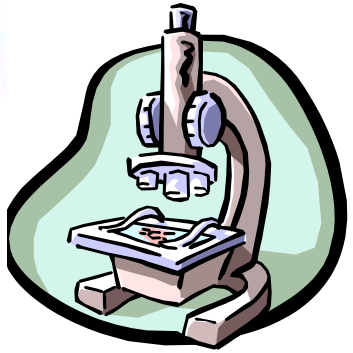
Chronic neuropathology

Alzheimer's disease
Huntington's disease
Parkinson's disease
Motoneuron disease

Basic Research

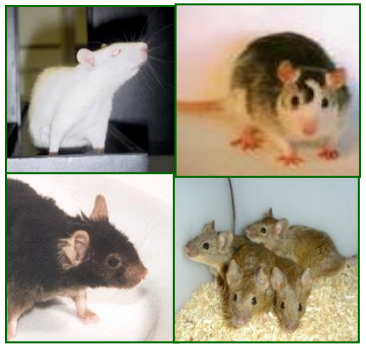


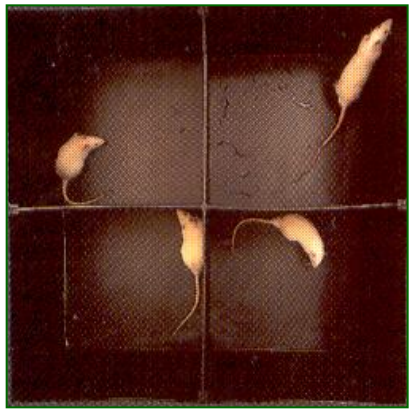
TOP DOWN

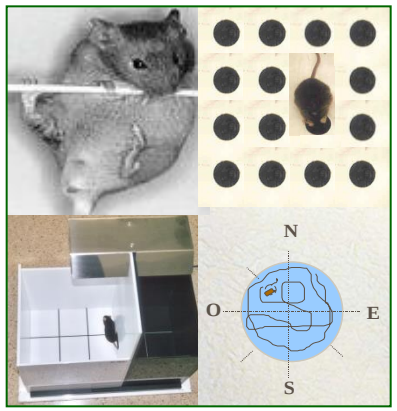


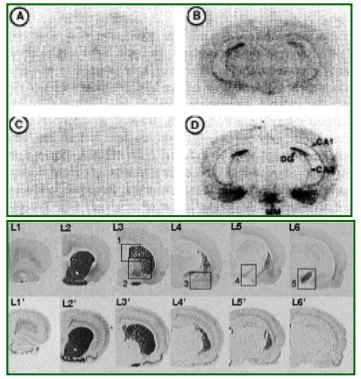
Levels of Study

Animal models of
Psychiatric and Neurological disorders

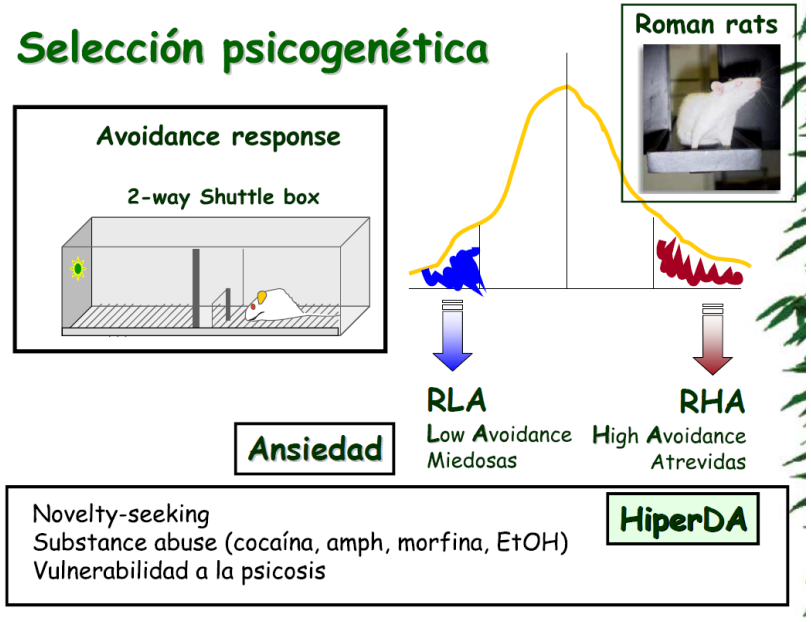






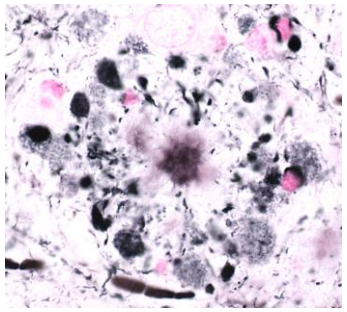


Selección psicogenética

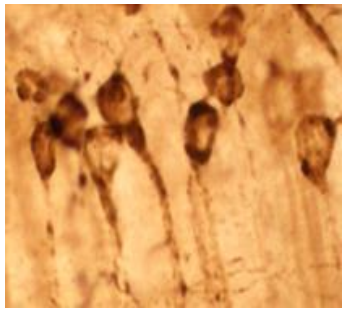


The model:
Who ?
What?
When?

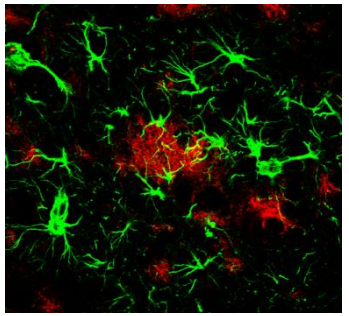
3xTgAD



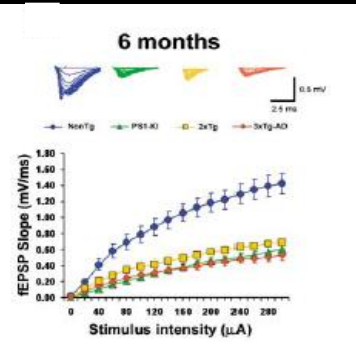
BA



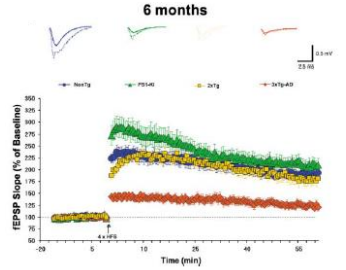
PHF



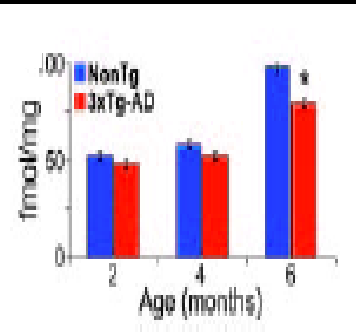
Gliosi



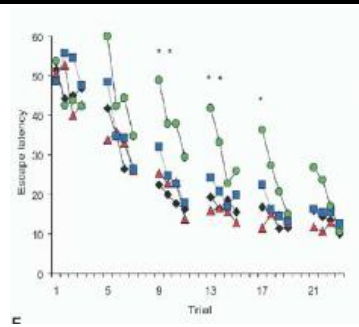
Def.fEPSP



Def.LTP



Def.a7nAChR



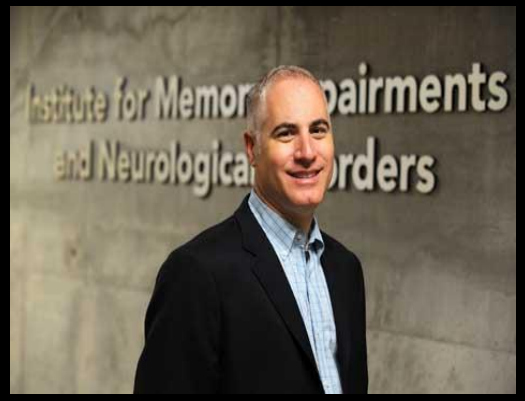
Def.L&M

Oddo *et al.* Frank M. LaFerla

University of California Irvine

Triple-transgenic of Alzheimer's disease with plaques and tangles: Intracellular AB and synaptic dysfunction.

Neuron 2003; 39



3xTgAD

PSD $_{M164V}$

APP $_{Swe}$

tau $_{P301L}$

Available online at www.sciencedirect.com
ScienceDirect
Neuroscience and Biobehavioral Reviews 31 (2007) 125–147
NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS
www.elsevier.com/locate/neubiorev

Review

Modeling behavioral and neuronal symptoms of Alzheimer's disease in mice: A role for intraneuronal amyloid

L. Giménez-Llort[a,*], G. Blázquez[a], T. Cañete[a], B. Johansson[b,c], S. Oddo[d], A. Tobeña[a], F.M. LaFerla[d], A. Fernández-Teruel[a]

[a]Medical Psychology Unit, Department of Psychiatry and Forensic Medicine, School of Medicine, Institute of Neuroscience, Autonomous University of Barcelona, 08193 Bellaterra, Barcelona, Spain
[b]Department of Neuroscience, Karolinska Institutet, KS CMM L8:01, SE-171 76 Stockholm, USA
[c]Department of Clinical Neuroscience, Karolinska Institutet, KS CMM L8:01, SE-171 76 Stockholm, Sweden
[d]Department of Neurobiology and Behavior, University of California, Irvine, CA 92697-4545, USA

Abstract

The amyloid Aβ-peptide (Aβ) is suspected to play a critical role in the cascade leading to AD as the pathogen that causes neuronal and synaptic dysfunction and, eventually, cell death. Therefore, it has been the subject of a huge number of clinical and basic research studies on this disease. Aβ is typically found aggregated in extracellular amyloid plaques that occur in specific brain regions enriched in nAChRs in Alzheimer's disease (AD) and Down syndrome (DS) brains. Advances in the genetics of its familiar and sporadic forms, together with those in gene transfer technology, have provided valuable animal models that complement the traditional cholinergic approaches, although modeling the neuronal and behavioral deficits of AD in these models has been challenging. More recently, emerging evidence indicates that intraneuronal accumulation of Aβ may also contribute to the cascade of neurodegenerative events and strongly suggest that it is an early, pathological biomarker for the onset of AD and associated cognitive and other behavioral deficits. The present review covers these studies in humans, in in vitro and in transgenic models, also providing more evidence that adult 3 × Tg-AD mice harboring $PS1_{M146V}$, APP_{Swe}, tau_{P301L} transgenes, and mimicking many critical hallmarks of AD, show cognitive deficits and other behavioral alterations at ages when overt neuropathology is not yet observed, but when intraneuronal Aβ, synaptic and cholinergic deficits can already be described.

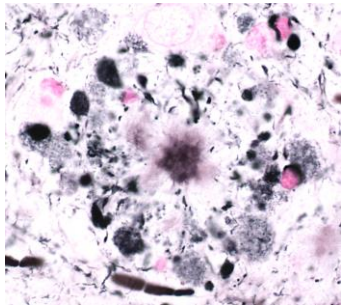
Keywords: Intraneuronal amyloid; Animal models; 3xTgAD mice; Learning and memory; Neuropsychiatric-like symptoms; Activity; Circadian rhythms; Emotion; Psychosis

Contents

*Corresponding author. Tel.: +34 93 581 2378; fax: +34 93 581 1435.
E-mail address: lidia.gimenez@uab.cat (L. Giménez-Llort).

0149-7634/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neubiorev.2006.07.007

3xTgAD



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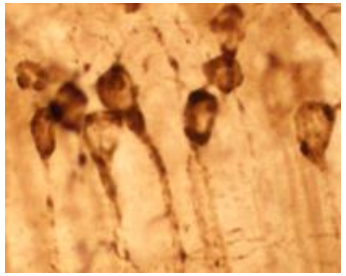
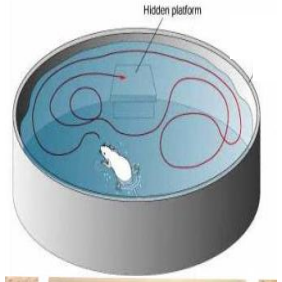
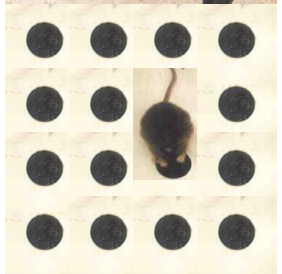


PHF

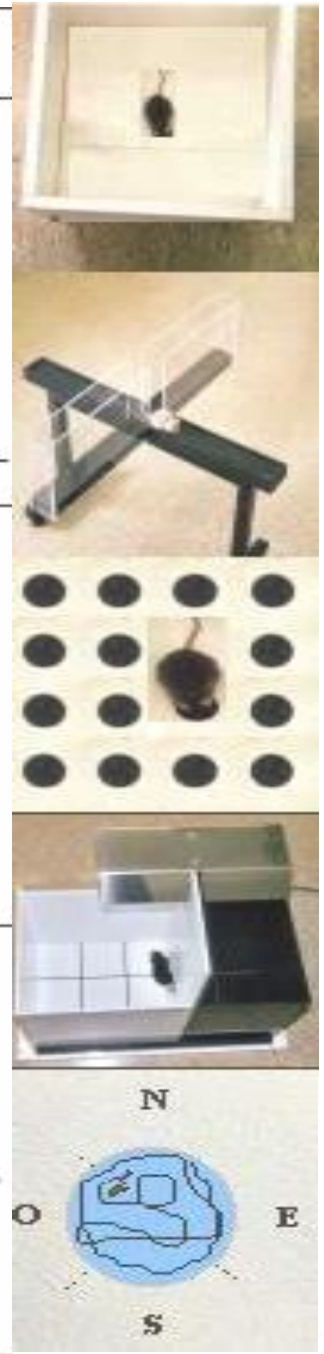
***PS1*M146V, *APP*Swe and *tau*P301L transgenes**



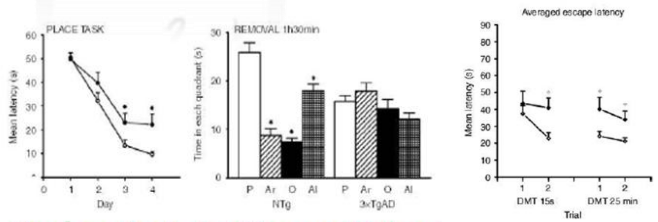


Behavioral screening of 3xTgAD mice

	Activity cages	Open-field	Plus-Maze or Corner test	Hole-board	Dark/light box
2.5 month-old	Total horizontal activity Total vertical activity	Total horizontal activity Total vertical activity	PM Entries OA Time in OA	Latency to explore Head-dips	Latency to white area Time in white area
6 month-old	Total horizontal activity Total vertical activity	Total horizontal activity Total vertical activity	PM Entries OA Time in OA	Latency Head-dips	Latency Time in white area
12 month-old	Total horizontal activity Total vertical activity	Total horizontal activity Total vertical activity	CT Number of corners Number of rearings	Latency Head-dips	Latency Time in lit area



Converger
Validity
Rethinking
Refinemer

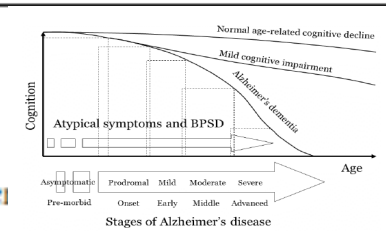


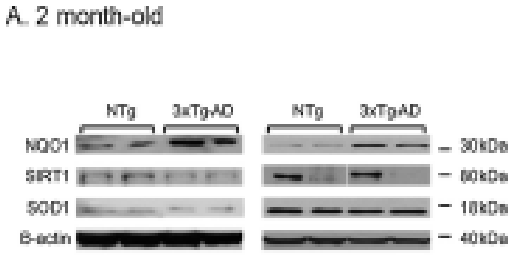
Giménez-Llort et al Neurosci Behav Rev 2006

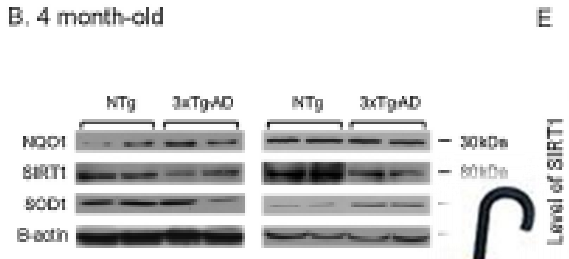
Glòria Blàzquez, Setembre 2006

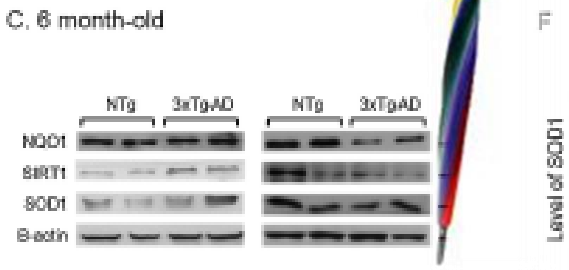
Table 1. Temporal course of behavioral changes observed in males and females of a Spanish colony of 3×Tg-AD versus NTg mice

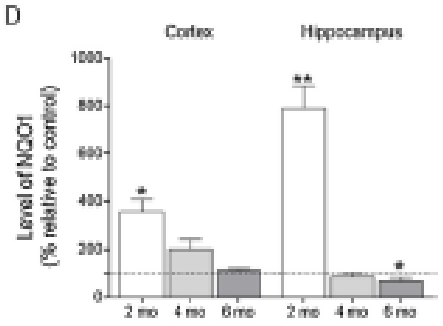
Giménez-Llort et al., 2014 Ann N Y Acad Sci. 2012

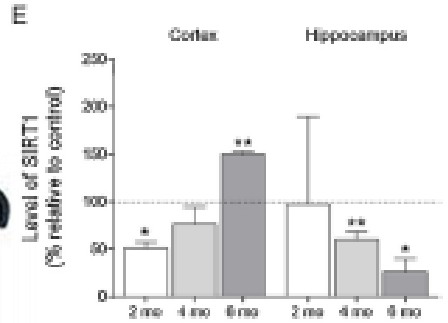
Behavior parameter 	Stages of neurodegeneration			
	Onset (2.5 m)	Early stages (4 m)	Moderate stages (6 m)	Advanced stages (12 m or more)
Increased sensorimotor function	n.s.	n.s.	+	++
BPSD-like symptoms				
Emotionality	+	+	++	+++
Neofobia	n.s.	+.	n.s.	+++
Reduced exploration in ansiogenic places	+	++	++	+++
Anxiety-like behaviors	+	++	++	+++
Hyperactivity	n.s.	+	+	++
Desinhibition	n.s.	n.a.	++	n.s.
Impulsivity	n.s.	n.a.	+	+++
Reduced novelty seeking	n.s.	n.a	n.s.	n.a.
Dysfunction of startle response	n.a.	n.a.	+	n.a.
Dysfunction of prepulse inhibition	n.a.	n.a.	+	n.a.
Cognition				
Spatial Working memory deficits	n.s.	n.a.	+	+++
Spatial Short-term memory deficits	n.s.	n.a.	n.s.	+++
Spatial Long-term memory deficits	n.s.	+	++	+++
Instrumental conditioning deficits	n.a.	n.a.	++	n.a.
Alteration Circadian rhythms	n.a.	n.a.	+	+++

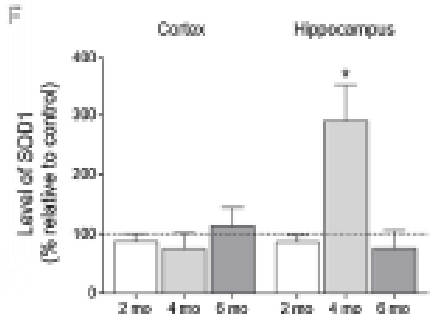












Behavioural Brain Research 271 (2014) 140–146

Contents lists available at ScienceDirect

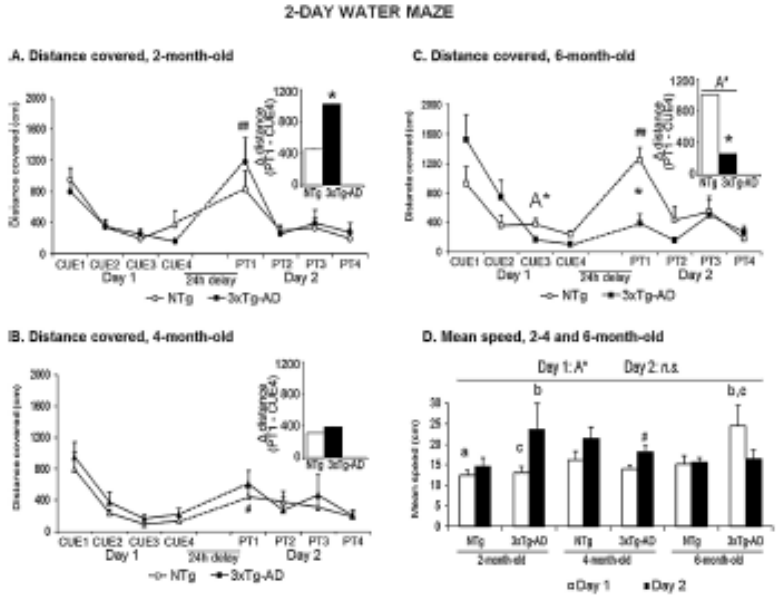
Behavioural Brain Research

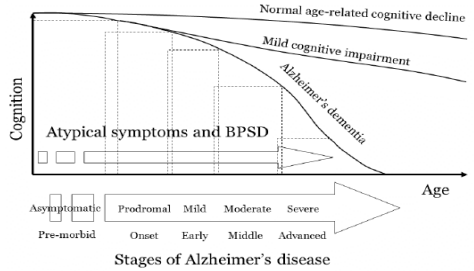
journal homepage: www.elsevier.com/locate/bbr

Short Communication

Neophobia, NQO1 and SIRT1 as premorbid and prodromal indicators of AD in 3xTg-AD mice

Virginia Torres-Lista[a,b,1], Cristina Parrado-Fernández[c,d,1], Ismael Alvarez-Montón[a,b], Javier Frontiñán-Rubio[c], Mario Durán-Prado[c,d], Juan Ramón Peinado[c,d], Björn Johansson[e], Francisco Javier Alcaín[c,d,*], Lydia Giménez-Llort[a,b,**]



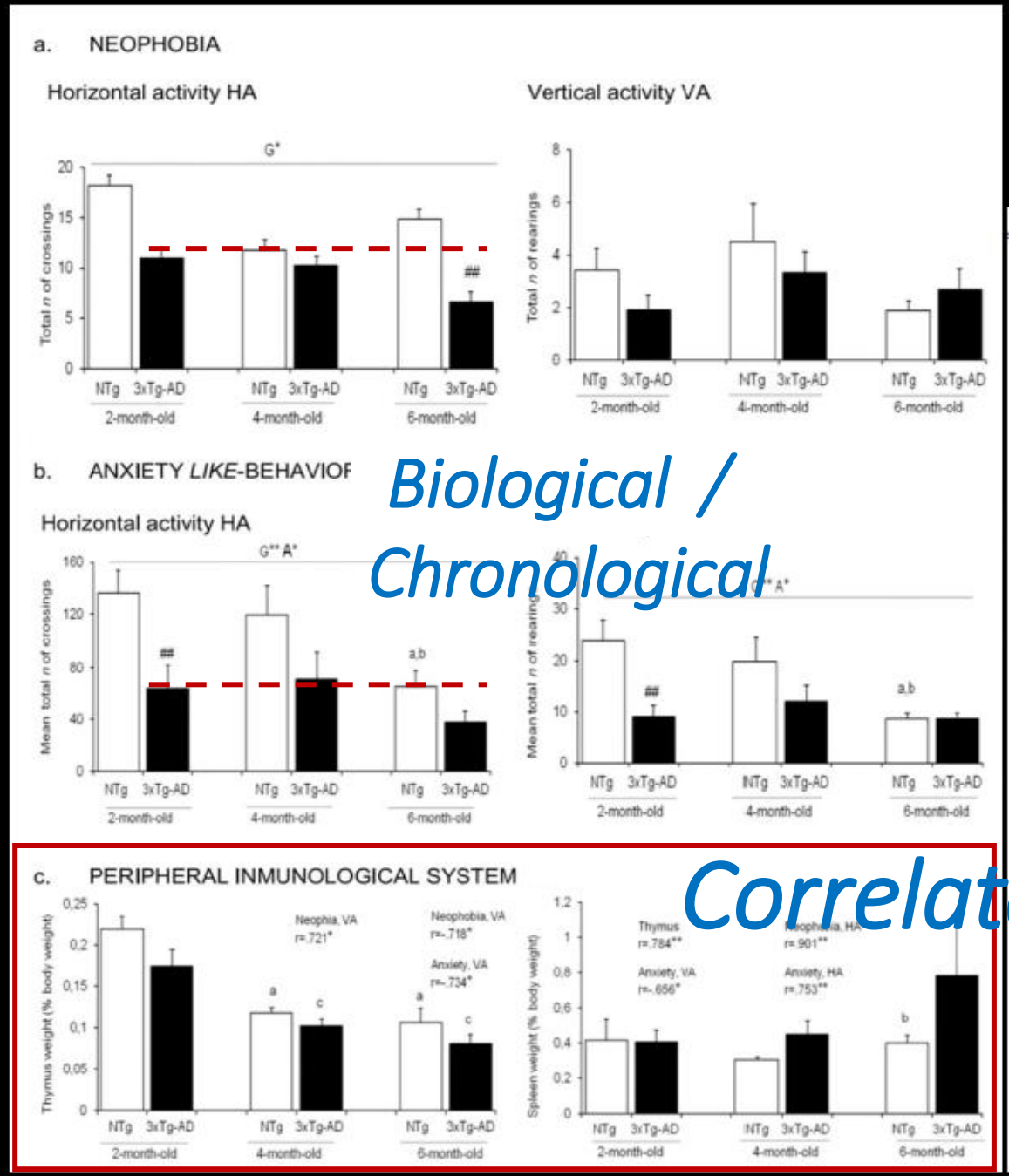


- Latency of rearing was the first behavioral indicator of premorbid AD (Pm-AD).
- Prodromal AD was clearly defined by cognitive deficits at 6 months of age.
- High levels of cortical and hippocampal NQO1 were a redox indicator of Pm-AD.
- SOD1 was changed only in hippocampus at 4 months of age, before prodromal AD.
- SIRT1 levels had opposite regional and temporal premorbid/prodromal patterns.

Crosstalk between

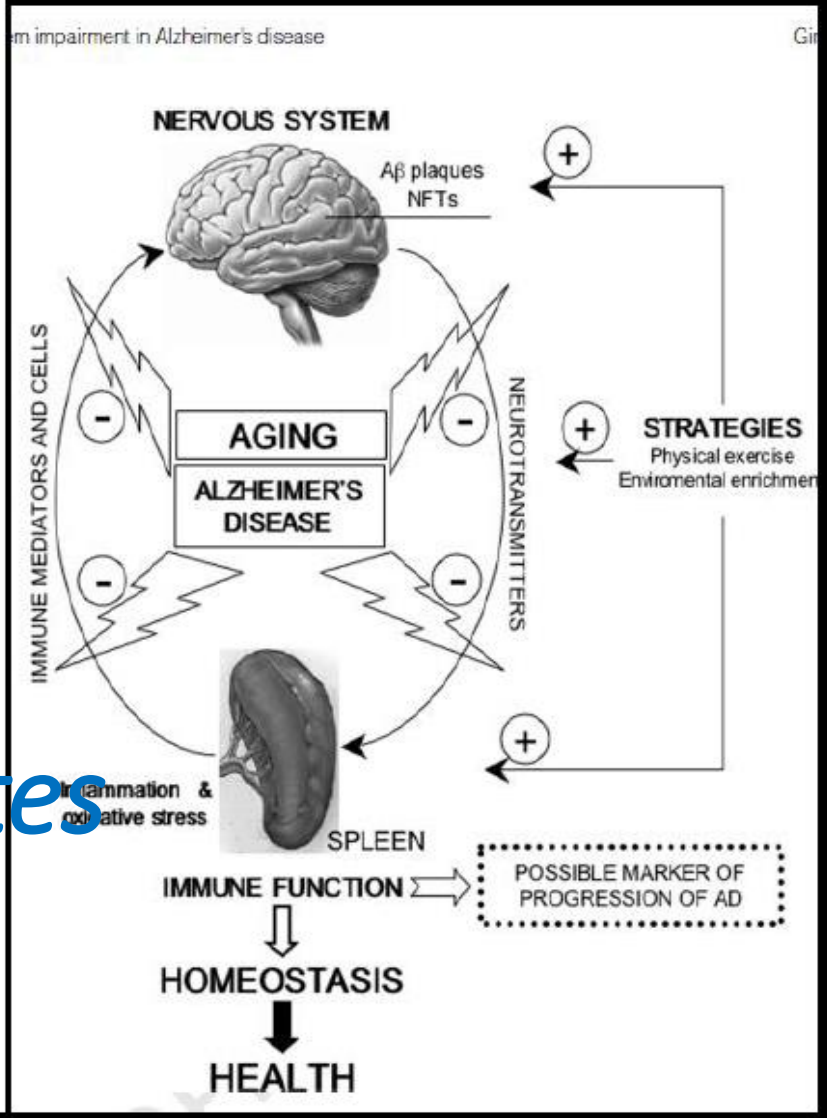
Behavior and Immune System in AD

Giménez-Llort et al., Current Pharmaceutical Design, 2014



Biological / Chronological

Correlates



Mortality rates · Survival bias

NeuroImmunoModulation

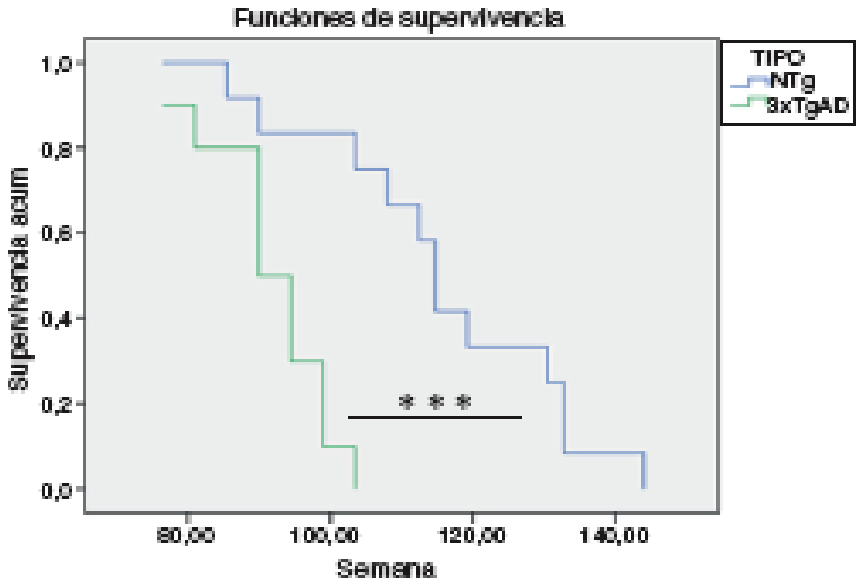
Neuroimmunomodulation 2008;15:331–343
DOI: 10.1159/000156475

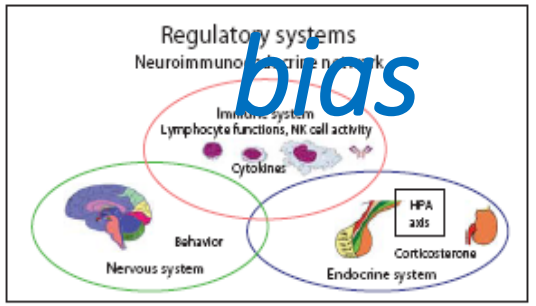
Published online: November 26, 2008

Gender-Specific Neuroimmunoendocrine Aging in a Triple-Transgenic 3×Tg-AD Mouse Model for Alzheimer's Disease and Its Relation with Longevity

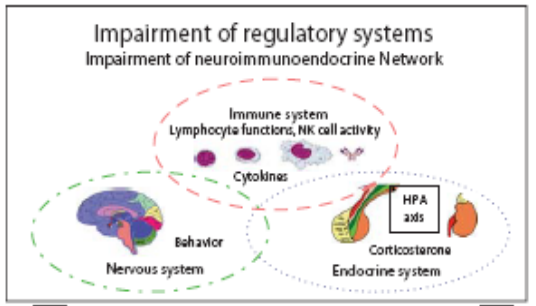
Lydia Giménez-Llort[a] Lorena Arranz[b] Ianire Maté[b] Mónica De la Fuente[b]

[a]Department of Psychiatry and Forensic Medicine, Institute of Neuroscience, Autonomous University of Barcelona, Bellaterra, and [b]Department of Physiology (Animal Physiology II), Faculty of Biology, Complutense University of Madrid, Madrid, Spain

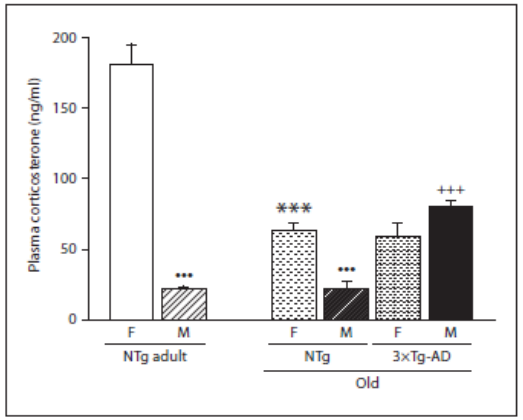




Aging
AD (3×Tg-AD mice)
(Gender differences)



Impairment of homeostasis
Increase in morbidity and mortality



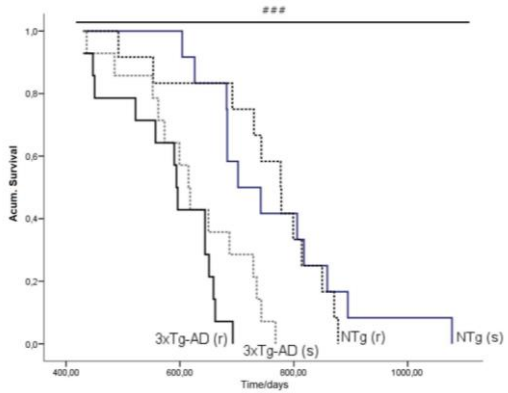
Journal of Alzheimer's Disease Reports 1 (2017) 47–57
DOI 10.3233/ADR-170011
IOS Press

Survival Curves and Behavioral Profiles of Female 3xTg-AD Mice Surviving to 18-Months of Age as Compared to Mice with Normal Aging

Virginia Torres-Lista[a,b], Mónica De la Fuente[c,d] and Lydia Giménez-Llort[a,b,*]

Impact of Chronic Risperidone Use on Behavior and Survival of 3xTg-AD Mice Model of Alzheimer's Disease and Mice With Normal Aging

Virginia Torres-Lista[1,2], Secundi López-Pousa[3] and Lydia Giménez-Llort[1,2]*



biomedicines

MDPI

Article

Survival Bias and Crosstalk between Chronological and Behavioral Age: Age- and Genotype-Sensitivity Tests Define Behavioral Signatures in Middle-Aged, Old, and Long-Lived Mice with Normal and AD-Associated Aging

Lydia Giménez-Llort [1,2,*,†], Daniela Marin-Pardo [1,2,†], Paula Marazuela [3] and Mar Hernández-Guillamón [3]

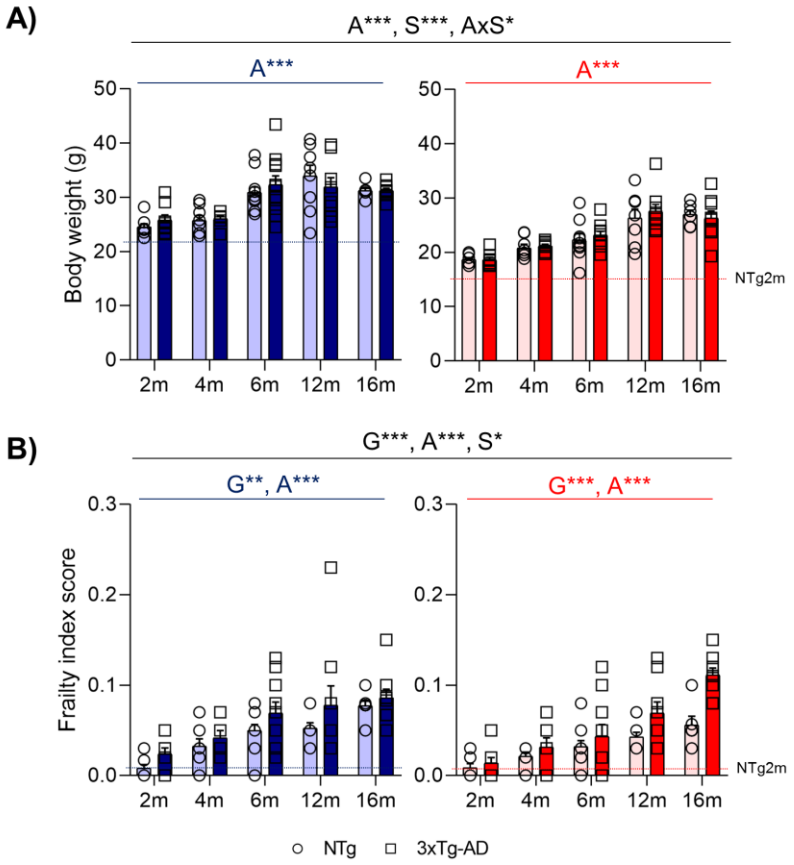
Behavioral Tests and Variables	G	A	S
Corner test (CT)			
Total visited corners	*	**	**
Total numbers of rearings	-	-	-
Latency of rearing (s)	-	-	-
Open field test (OF)			
Freezing- Latency of first movement (s)	-	*	-
Latency to exit the center (s)	-	-	-
Latency to entering the peripheral ring (s)	-	***	-
Latency of rearing (s)	***	***	-
Latency of self-grooming (s)	-	-	-
Total horizontal activity (*n* crossings)	*	***	-
"in the center (*n* crossings)	-	*	*
"in the periphery (*n* crossings)	*	***	-
Total vertical activity (*n* of rearings)	*	***	*
Gait analysis- Total number of pauses	-	***	-
Gait analysis- Mean number of crossings	***	*	-
Defecation (n)	*	-	-
Urination (%)	-	-	***
Context and object recognition tests			
OF2- Freezing- Latency of first movement (s)	-	***	-
OF2- Latency to exit the center (s)	***	***	-
OF2- Latency to entering the peripheral ring(s)	***	***	-
OF2- Latency of rearing (s)	*	**	-
OF2- Latency of self-grooming (s)	-	-	-
OF2- Total horizontal activity	*	*	-
OF2- "in the center (*n* of crossings)	*	-	-
OF2- "in the periphery (*n* of crossings)	-	*	-
OF2- Total vertical activity (*n* of rearings)	-	*	-
OF2- Urination (%)	-	-	***
OR Sample trial- Time exploring object (s)	-	*	-
OR-Sample trial- Time to reach the criteria (s)	-	-	-
OR- Test trial- Object latency (s)	*	-	-
Marble test (MB)			
Intact (n)	-	*	-
Buried (n)	-	***	-
Spontaneous alternation in the T-Maze test			
Latency of first movement (s)	-	***	-
Latency to cross the intersection (s)	-	*	*
Total time to complete the test (s)	-	-	-
Total number of errors (*n*)	*	**	-
T-Maze test			
Latency of first movement (s)	*	-	-
Test trial- Latency to cross the intersection (s)	**	-	-
Test trial- time to complete the test (s)	**	-	-
Morris water maze test (MWM)			
Escape latency - CUE	-	-	-
Escape latency - PT1	-	-	-
Escape latency - PT2	-	-	-
Escape latency - PT3	**	**	-
Escape latency - PT4	*	***	-
Distance - CUE	-	-	*
Distance - PT1	-	-	-
Distance - PT2	-	-	-
Distance - PT3	-	**	-
Distance - PT4	-	***	-
Swimming speed - CUE	***	***	-
Swimming speed - PT1	***	**	-
Swimming speed - PT2	**	**	-
Swimming speed - PT3	-	***	-
Swimming speed - PT4	*	**	-
Probe trial- Opposite quadrant distance (m)	-	***	-
Probe trial- Target quadrant distance (m)	*	-	-
Probe trial- Latency to platform (s)	*	-	-
Physical status			
Body Weight (g)	-	***	***
Frailty index	***	***	*

As shown in most behavioral variables, behavioral performances were strongly dependent on age.

Genotypes differed in their horizontal and vertical activities, thigmotaxis, coping with stress strategies, working memory, and frailty index.

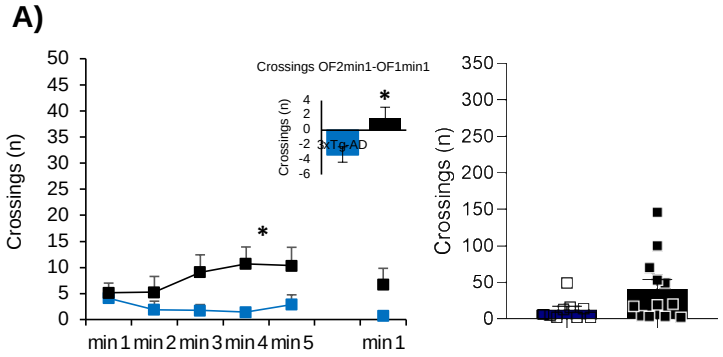
Sex effect was predominantly observed in a classical emotional variable and physical status, but also the horizontal and vertical activity in the test of neophobia and the open field.

PHYSICAL STATUS

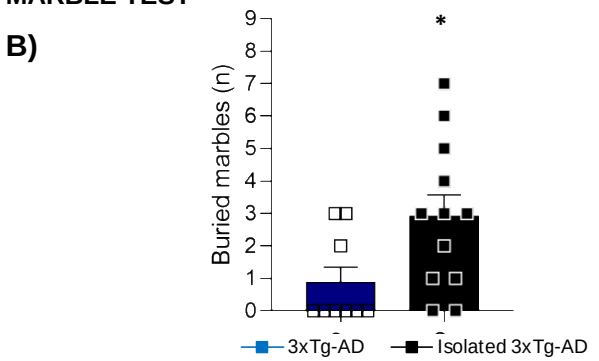


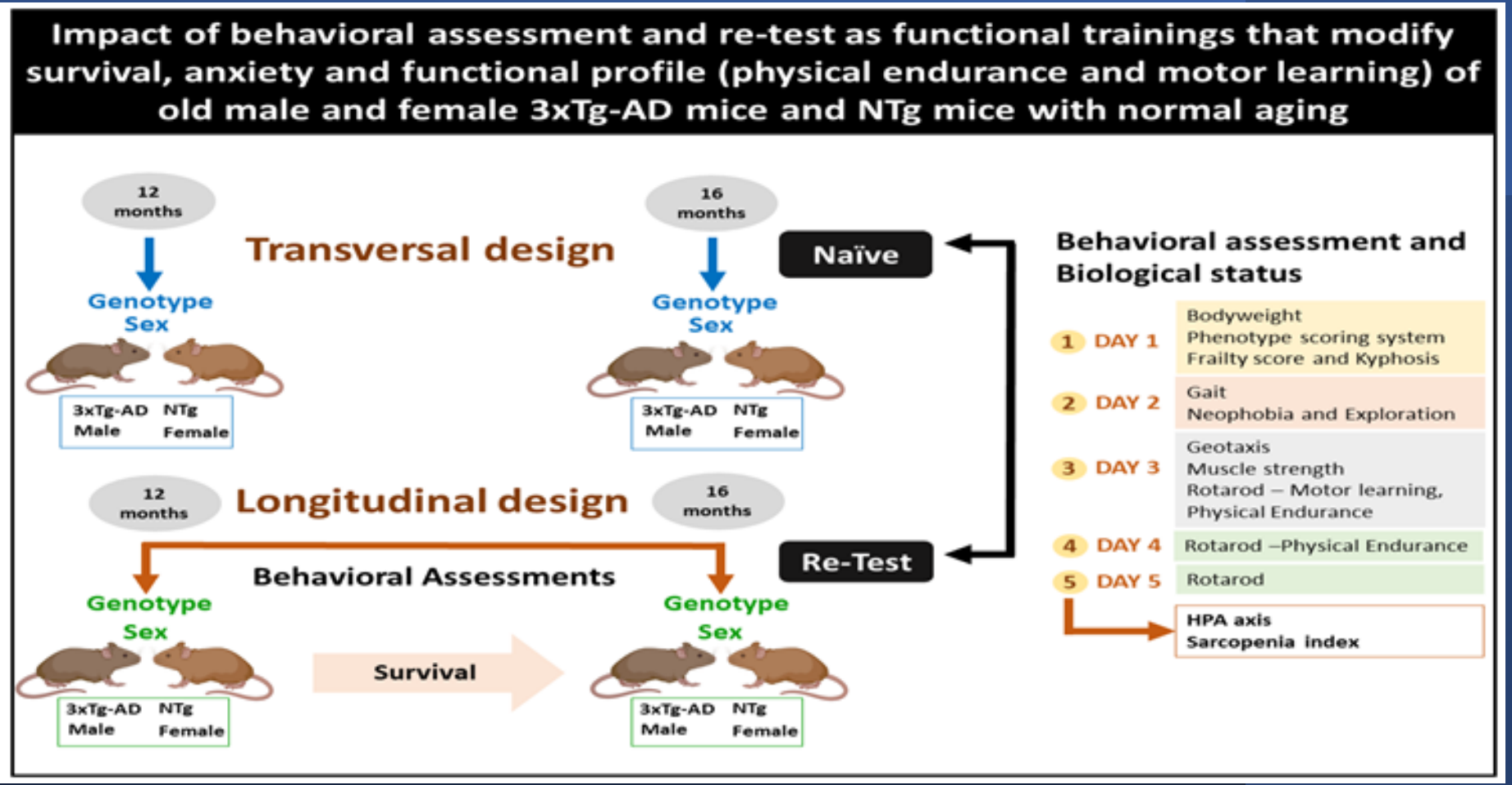
SOCIAL ISOLATION IMPACT ON 3xTg-AD

OPEN FIELD TEST

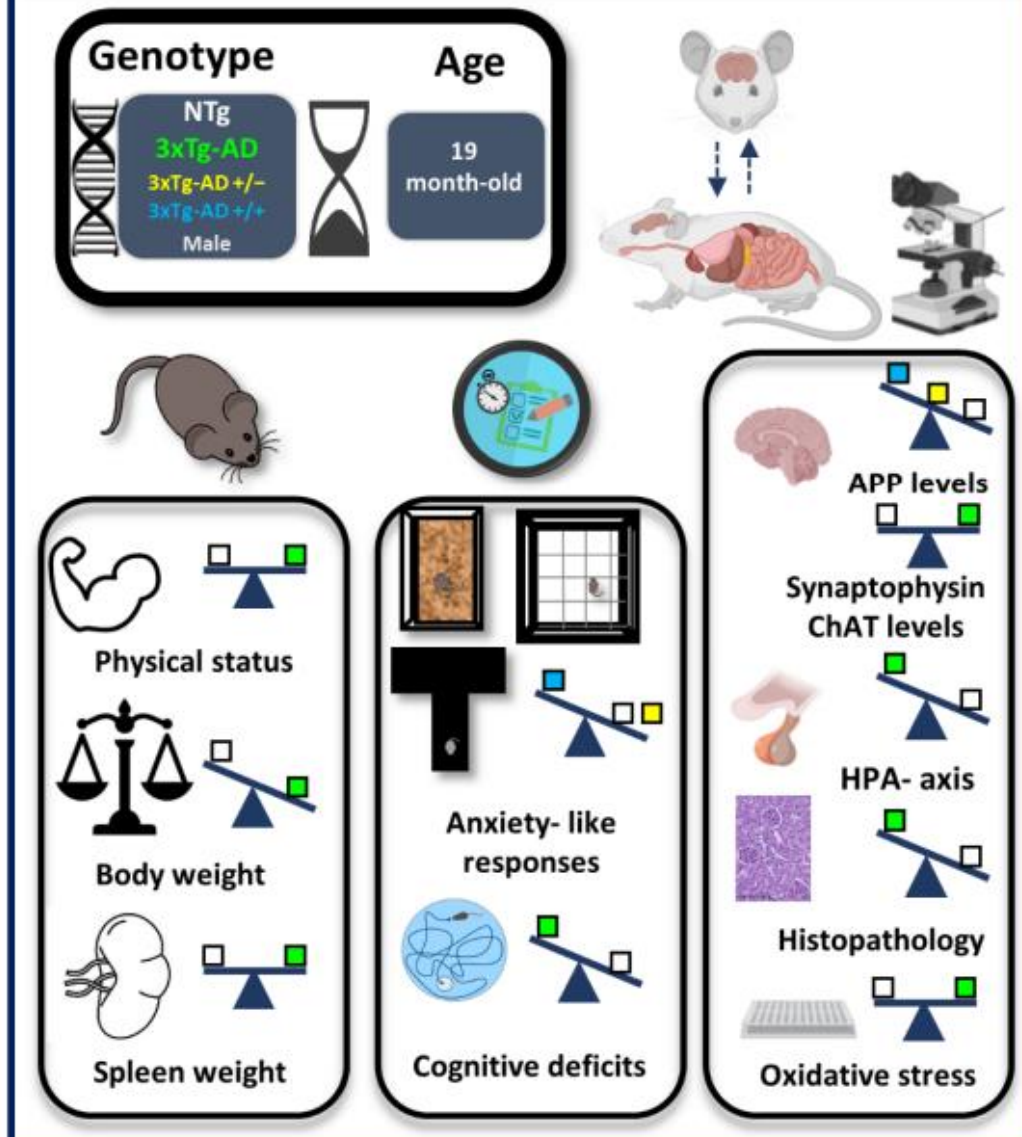


MARBLE TEST




Impact of behavioral assessment and re-test as functional trainings that modify survival, anxiety and functional profile (physical endurance and motor learning) of old male and female 3xTg-AD mice and NTg mice with normal aging
12 months
Transversal design
16 months
Naïve
Genotype
Sex
Genotype
Sex
3xTg-AD Male
NTg Female
3xTg-AD Male
NTg Female
12 months
Longitudinal design
16 months
Re-Test
Behavioral Assessments
Genotype
Sex
Genotype
Sex
Survival
3xTg-AD Male
NTg Female
3xTg-AD Male
NTg Female
Behavioral assessment and Biological status
1 DAY 1
Bodyweight
Phenotype scoring system
Frailty score and Kyphosis
2 DAY 2
Gait
Neophobia and Exploration
3 DAY 3
Geotaxis
Muscle strength
Rotarod – Motor learning, Physical Endurance
4 DAY 4
Rotarod –Physical Endurance
5 DAY 5
Rotarod
HPA axis
Sarcopenia index

Genotype load modulates amyloid burden and anxiety-like patterns in male 3xTg-AD survivors despite similar neuro-immunoendocrine, synaptic and cognitive impairments.



INc Institut de Neurociències UAB

"Genotype load modulates amyloid burden and anxiety-like patterns in male 3xTg-AD survivors despite similar neuro-immunoendocrine, synaptic and cognitive impairments"

Departament de Psiquiatria i Medicina Legal UAB

STUDY 3

3xTg-AD+/+
3xTg-AD+/-
NTg
♂
19 months old

BEHAVIORAL PHENOTYPE

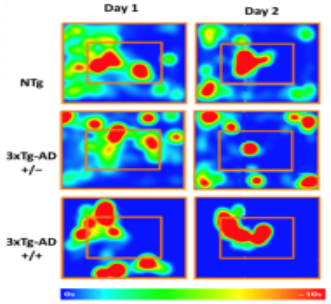
SYSTEMIC PHENOTYPE

NEUROPATHOLOGY

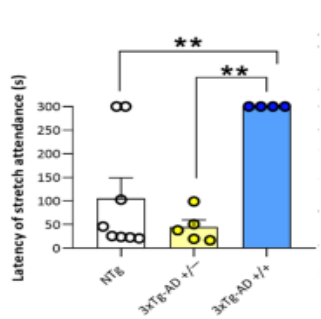
BEHAVIORAL PHENOTYPE

Survival Bias: Convergence of behavioral profile. Cognitive impairment the salient trait
Genotype: Anxiety-like profile more related to genetic load

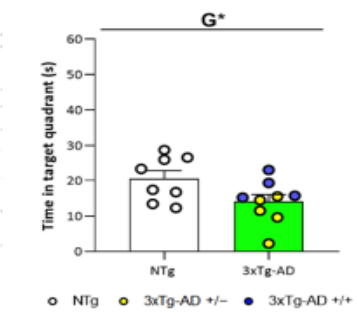
OF test



DL box test



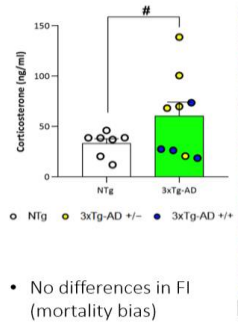
MWM test



Non-linear impact of genetic load in the different dimensions studied

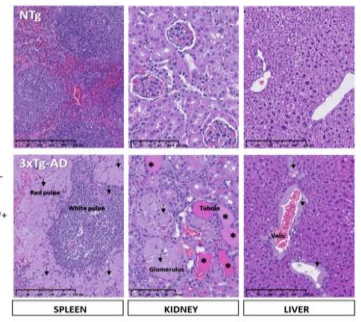
SYSTEMIC PHENOTYPE

HPA-axis



- No differences in FI (mortality bias)
- Non-linear increase of corticosterone levels

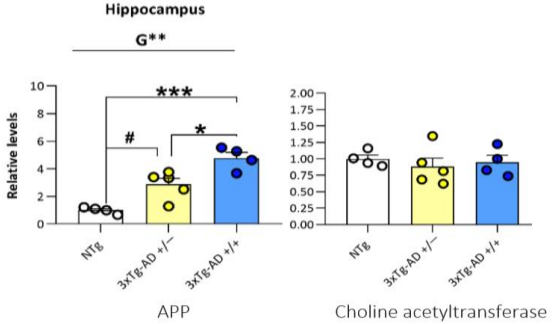
Histology



Histopathology provided evidence of the systemic features of AD, despite similar peripheral organs' oxidative stress

NEUROPATHOLOGY

Western Blot

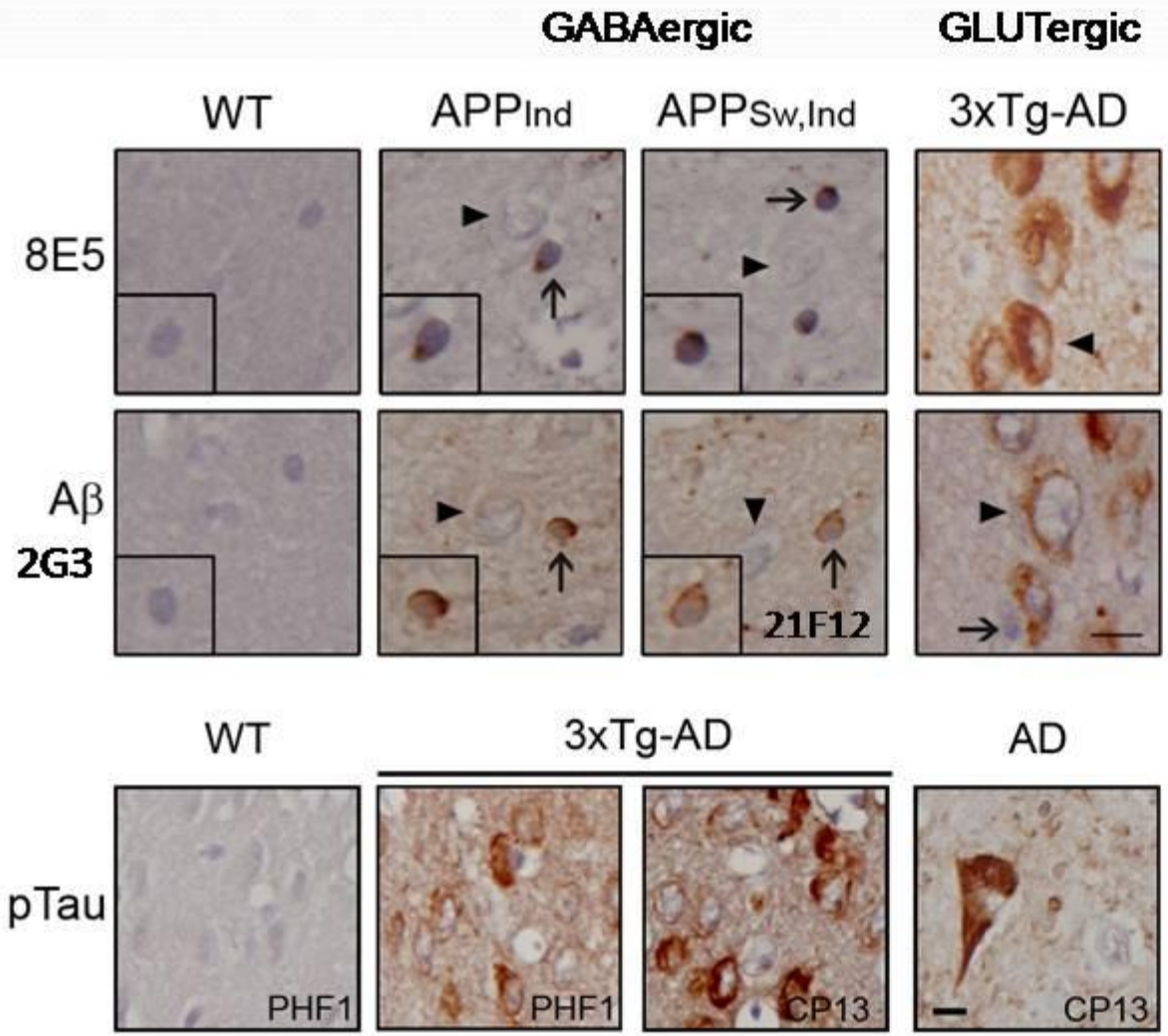


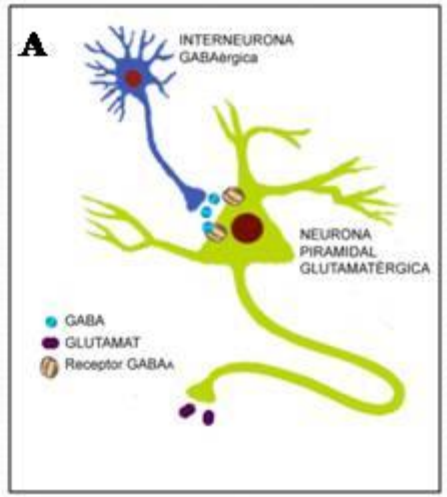
Increased APP
Convergent synaptophysin and choline acetyltransferase brain levels

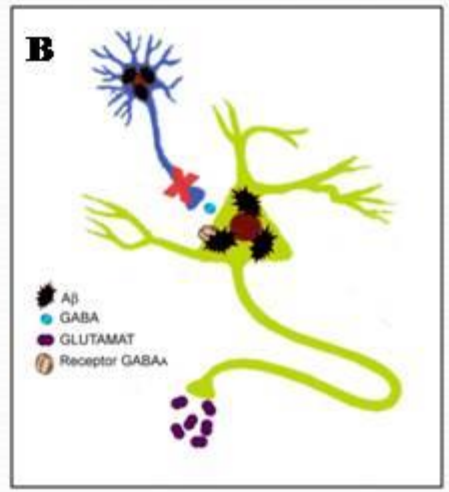
Non-linear impact of genetic load in the different dimensions studied

Muntsant et al. 2021

Intraneuronal Aβ accumulation in the basolateral amygdala of AD mice







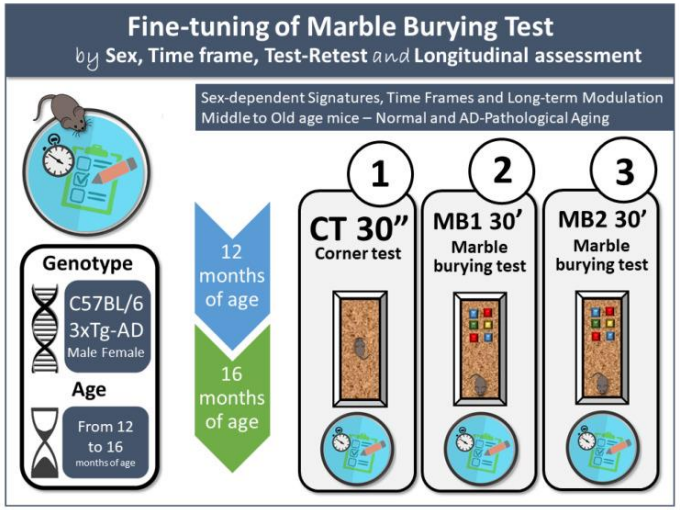
Behavioural Processes
Volume 116, July 2015, Pages 69-74

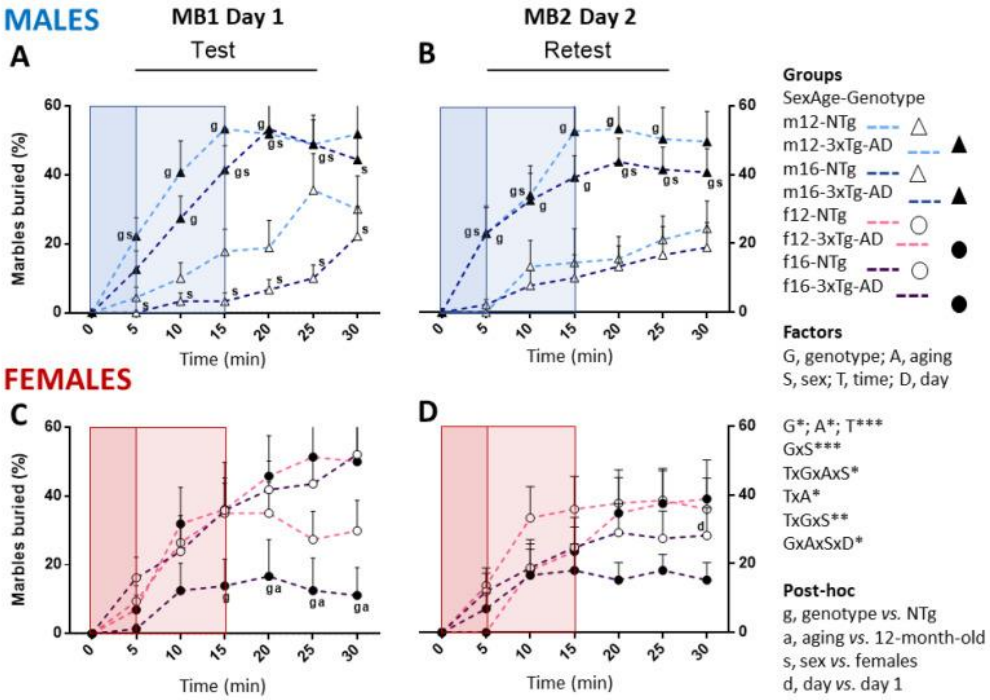
Short report

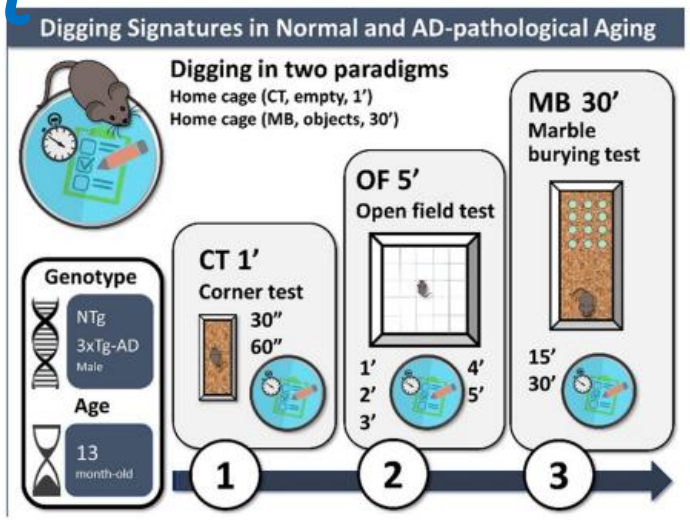
Marble-burying is enhanced in 3xTg-AD mice, can be reversed by risperidone and it is modulable by handling

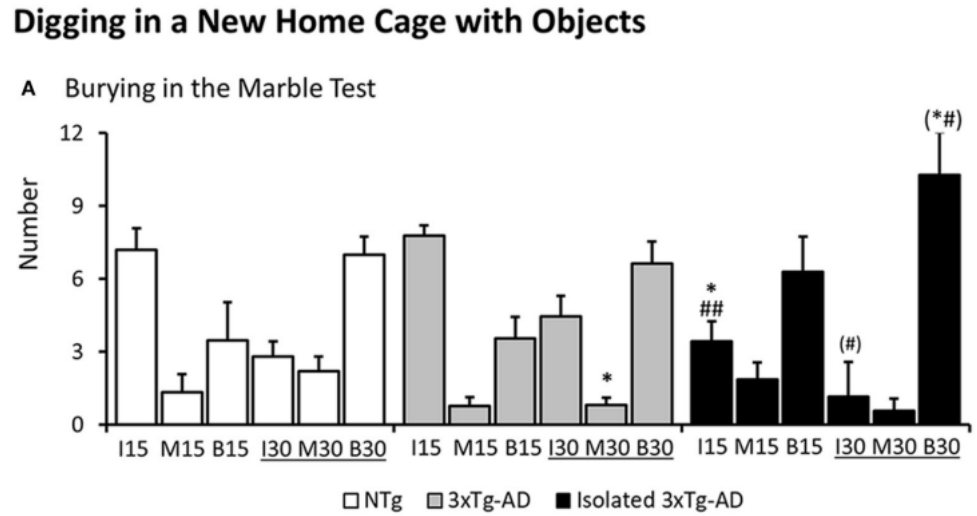
Virginia Torres-Lista [a b], Secundino López-Pousa [c], Lydia Giménez-Llort [a b]

Rethinking
Repurposing
Refinement

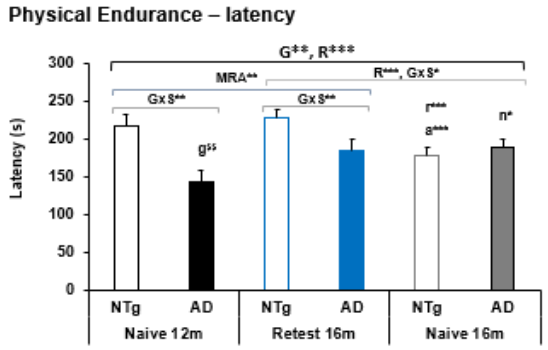


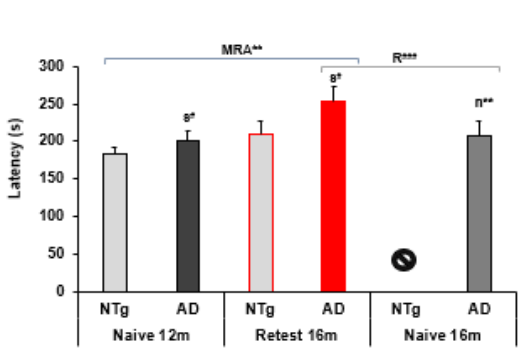


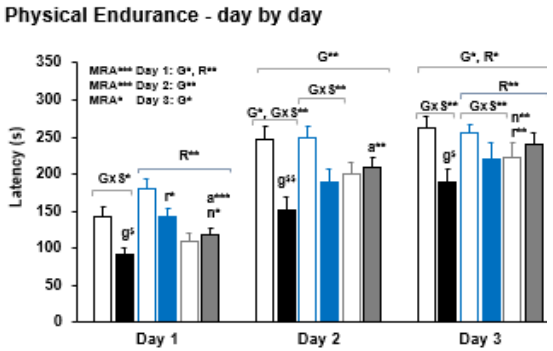


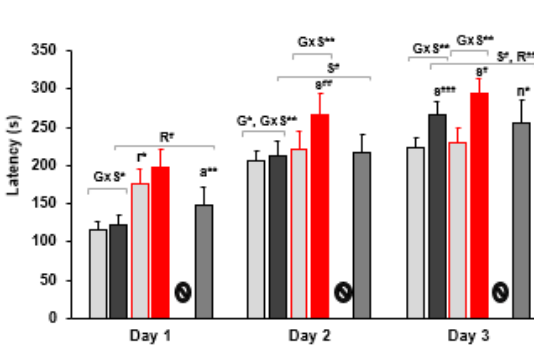


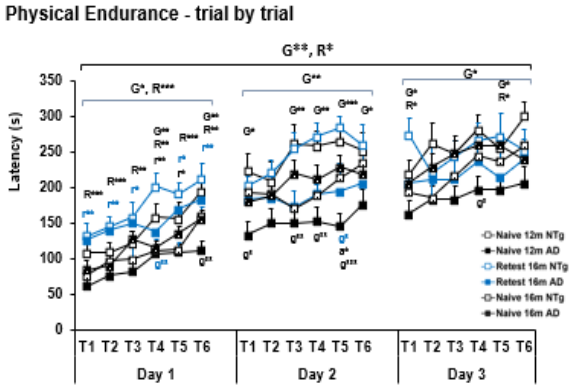
Motor learning and Physical Endurance - Rotarod

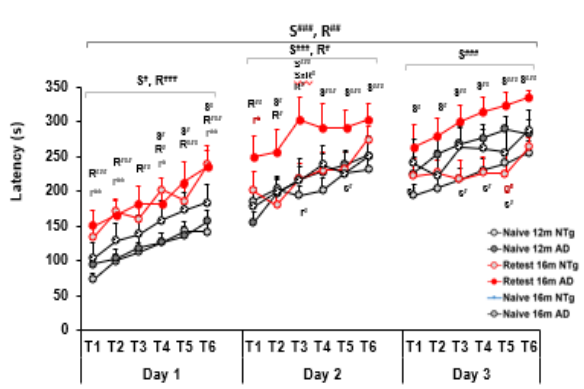


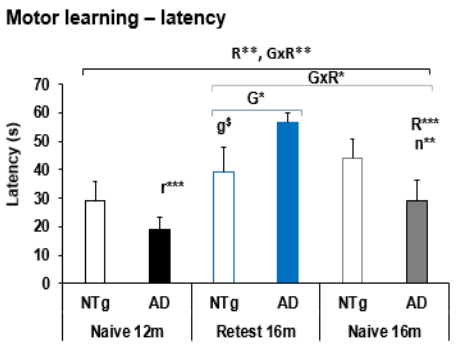


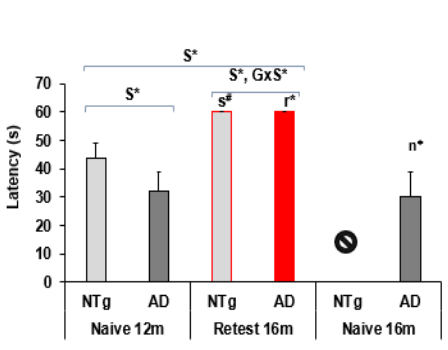


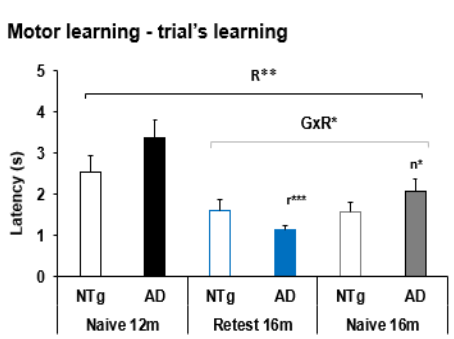


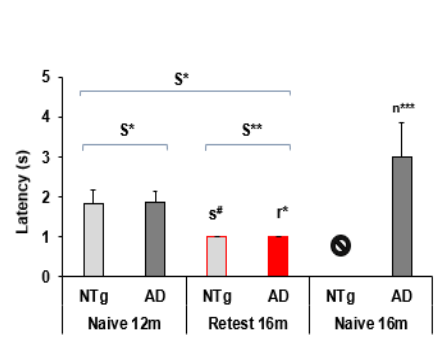












Males	Females
Naive 12m NTg	Naive 12m NTg
Naive 12m AD	Naive 12m AD
Retest 16m NTg	Retest 16m NTg
Retest 16m AD	Retest 16m AD
Naive 16m NTg	Naive 16m AD
Naive 16m AD	

Rethinking
Repurposing
Refinement

DOI: 10.3390/biomedicines10050973

Behavioural Brain Research 258 (2014) 97–105

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/bbr

Research report

Bizarre behaviors and risk assessment in 3xTg-AD mice at early stages of the disease

R. Baeta-Corral[a,b], L. Giménez-Llort[a,b,*]

[a] Institute of Neuroscience, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain
[b] Department of Psychiatry and Forensic Medicine, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

HIGHLIGHTS

- Bizarre behaviors in 3xTg-AD mice were conspicuous and measurable early-BPSD.
- They consisted in stereotyped-rearing and stretching, backward movements and jumps.
- Female gender was the most suitable to study bizarre movements and risk assessment.
- Handling reduced bizarre behaviors and freezing whereas potentiated risk assessment.
- Besides, handling induced selective effects on locomotor activity and emotionality.

Rethinking
Repurposing
Refinement

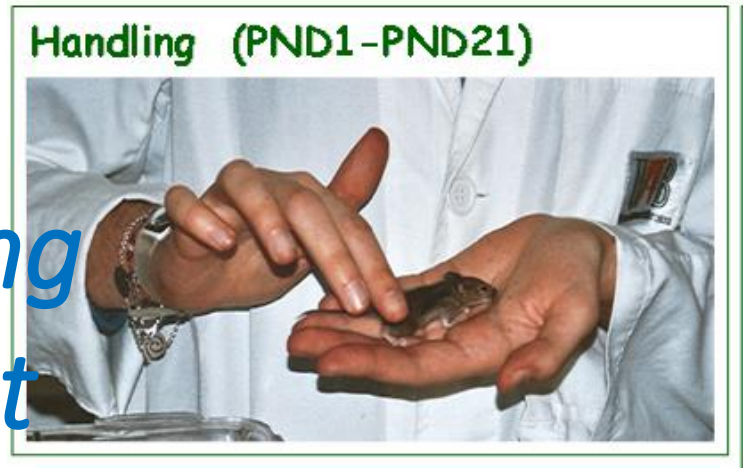


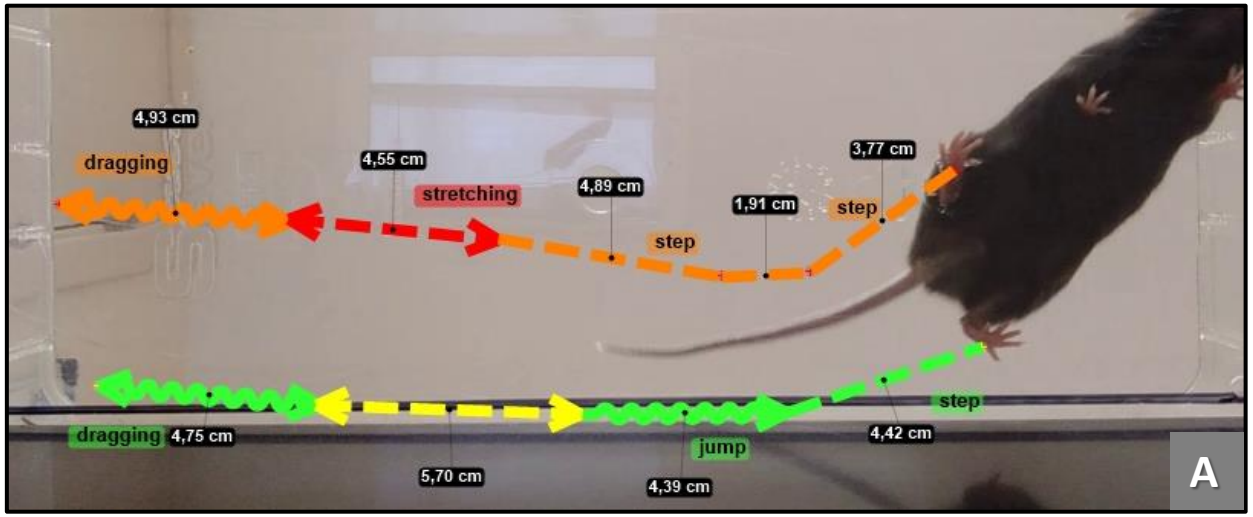
Table 1
Long-term effects of postnatal handling on bizarre behaviors elicited by 6-months-old C57BL/6 × 129 and 3xTg-AD mice in the open field test.

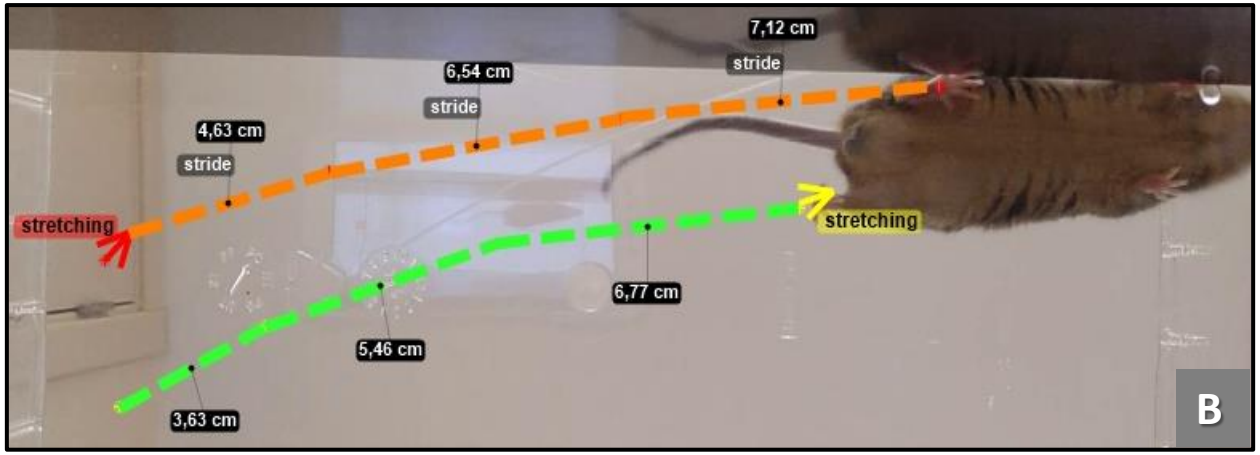
	Non-transgenic mice		3xTg-AD mice	
	Males	Females	Males	Females
Non-handled animals				
Stereotyped stretching	–	+	–	+
Stereotyped rearings	+++	+++	+++	++
Backward movements	–	+	–	+++
Jumping	+	–	–	–
Handled animals				
Stereotyped stretching	–	+	–	+
Stereotyped rearings	++	+	++	+
Backward movements	+	+	+	+
Jumping	–	–	–	–

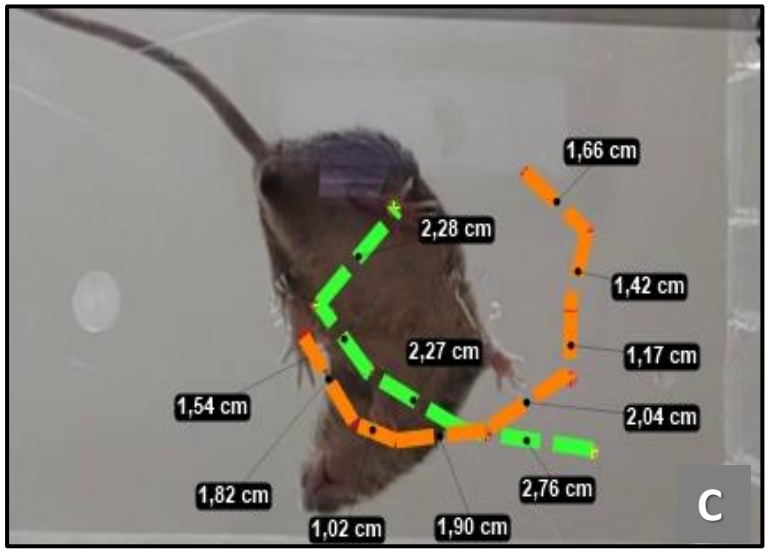
For each of the four bizarre behaviors, the results are expressed as the incidence (percentage, %) of animals exhibiting that behavior: 0%: (–); 0–33%: (+); 33–66%: (++); 66–100% (+++).

Refinement

Gait and Bizarre gait patterns







Gait patterns and trajectory (A), (B)

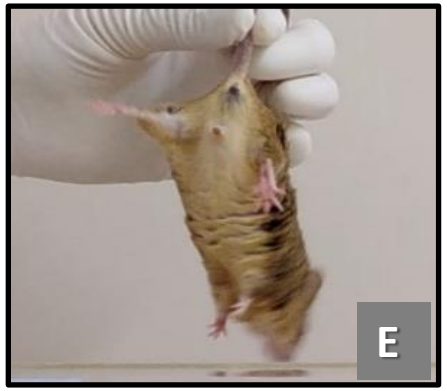
“Circling” bizarre gait pattern (C)

Castillo-Mariqueo L, Pérez-García MJ, Giménez-Llort L. Modeling Functional Limitations, Gait Impairments, and Muscle Pathology in Alzheimer's Disease: Studies in the 3xTg-AD Mice. Biomedicines. 2021;9(10):1365. Published 2021 Oct 1. doi:10.3390/biomedicines9101365

Refinement

Kyphosis and Hindlimb clasping

Structural Kyphosis: (A) Sagittal plane lateral view; (B) Front plane rear view; (C) Transverse plane top view.



Hindlimb clasping: (D) normal response, (E) moderate response, and (F) severe response

Castillo-Mariqueo L, Giménez-Llort L. Clasping, ledge-score coordination and early gait impairments as primary behavioural markers of functional impairment in Alzheimer's disease. Behav Brain Res. 2022;435:114054. doi:10.1016/j.bbr.2022.114054

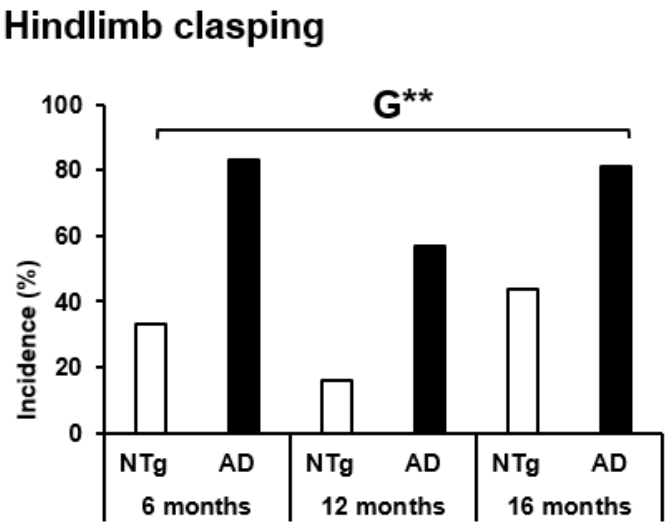
Experimental research

Modelling Functional Limitations, Gait Impairments, and Muscle Pathology

Conditions	NTg			3xTg-AD			Statistics
	6-months	12-months	16-months	6-months	12-months	16-months	
1. Survival (mean + SEM days) (mortality ratio)	329 + 25.26 3/15 (20%)	337 + 29.09 3/9 (33.3%)	350 + 15.60 20/40 (50%)	208 + 1.26 0/15 (0%)	395 + 9.63 1/16 (6.2%)	481 + 25.31 5/24 (20.8%)	S&&
2. Kyphosis (animals, %)	-	3/6 (50%)	5/9 (56%)	1/6 (17%)	3/7 (43%)	4/11 (36%)	A**
Postural	-	-	-	1/6 (17%)	-	1/11 (9%)	n.s.
Structural	-	3/6 (50%)	5/9 (56%)	-	3/7 (43%)	3/11 (27%)	A*
3. Physical conditions (animals, %)							
Body weight	30 g.	30 g.	30 g.	28 g.	33 g.	34g.	A*, a#
Alopecia	2/6 (33%)	4/6 (67%)	5/9 (56%)	1/6 (17%)	4/7 (57%)	4/11 (36%)	n.s.
Body position	-	-	-	-	-	5/11 (45%)	a#
Palpebral closure	-	-	-	-	-	4/11 (36%)	a#
Piloerection	-	1/6 (17%)	2/9 (22%)	-	-	6/11 (55%)	A*
Tail position	-	-	-	-	-	4/11 (36%)	a#
Tremor	-	1/6 (17%)	-	-	-	9/11 (82%)	A**, G*

Kaplan-Meier, Log Rank: S&& $p<0.01$. X_2, A: age, ** $p < 0.01$ * $p < 0.05$, G: genotype, * $p < 0.05$. n.s. $p > 0.05$.

- Signs of physical frailty accompany functional deterioration in these animals.



- The hindlimb clasping reflex is also a primary impairment indicating worsening AD symptomatology, present in 3xTg-AD mice regardless of age.

Castillo-Mariqueo - DOI: 10.3390/biomedicines9101365

Refinement: Who an When

Behavioural Brain Research 281 (2015) 156–171

Contents lists available at ScienceDirect

Behavioural Brain Research

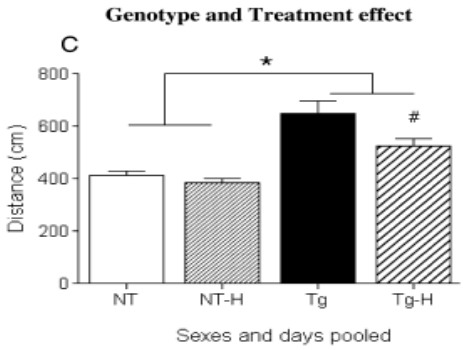
journal homepage: www.elsevier.com/locate/bbr

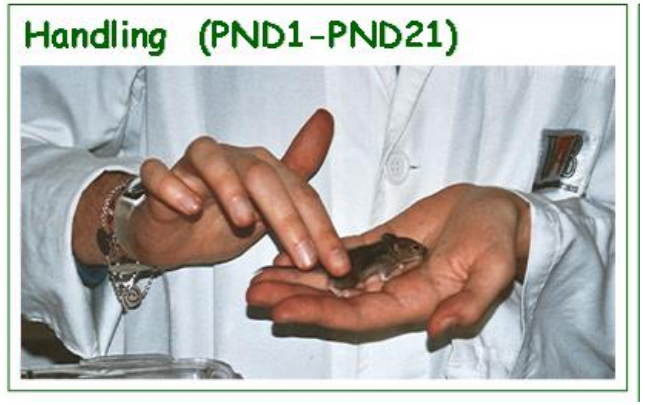
Research report

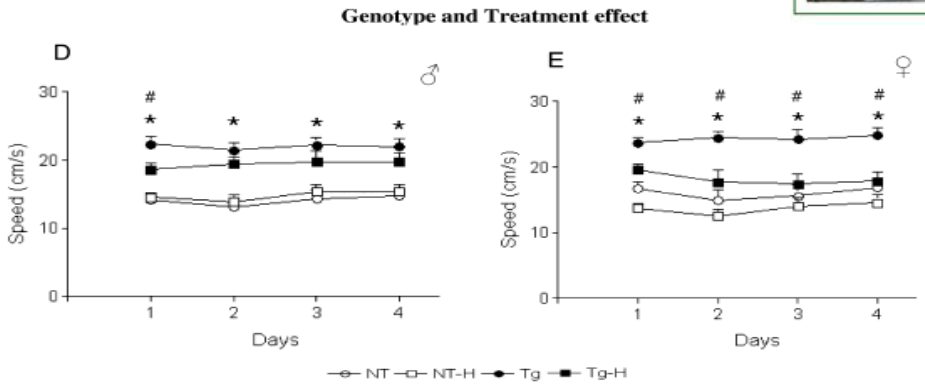
Cognitive and emotional alterations in young Alzheimer's disease (3xTgAD) mice: Effects of neonatal handling stimulation and sexual dimorphism

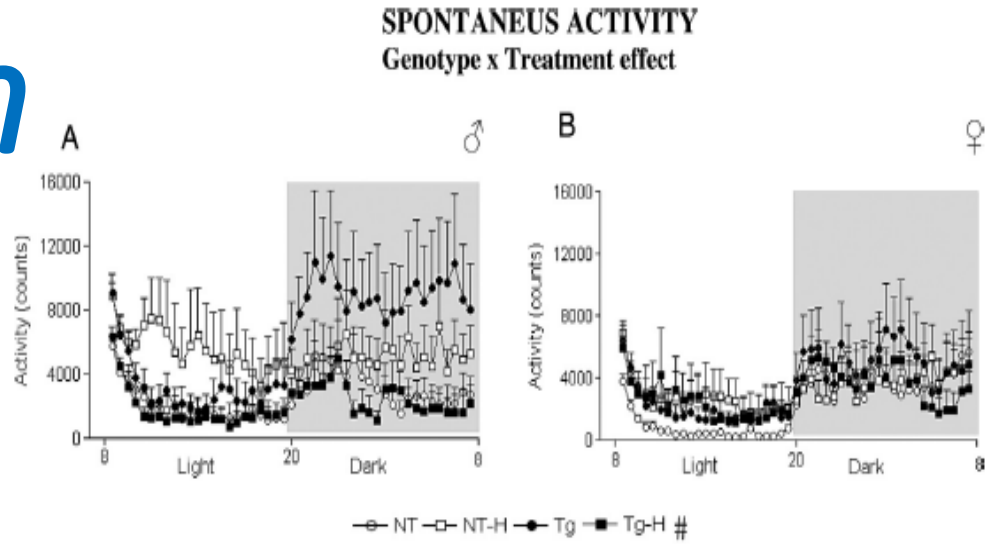
T. Cañete*, G. Blázquez, A. Tobeña, L. Giménez-Llort, A. Fernández-Teruel*

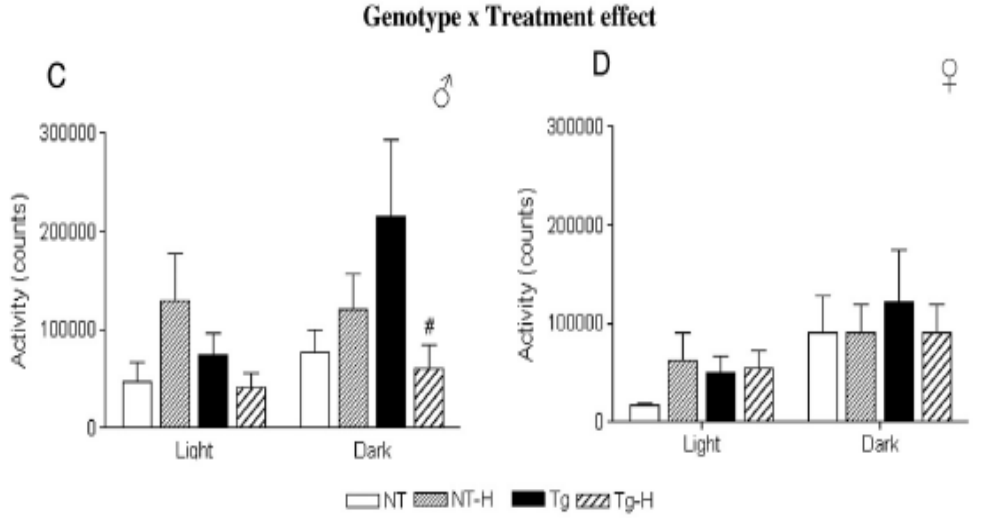
- Young 3xTgAD mice exhibit a spatial learning and reference memory deficit.
- 3xTgAD mice exhibit increased behavioral inhibition in some novelty tests.
- Sexual dimorphism appears in most novelty tests.
- Gender differences are reflected by increased cognitive deficits in females.
- Neonatal Handling improves spatial learning and normalize motor activity.

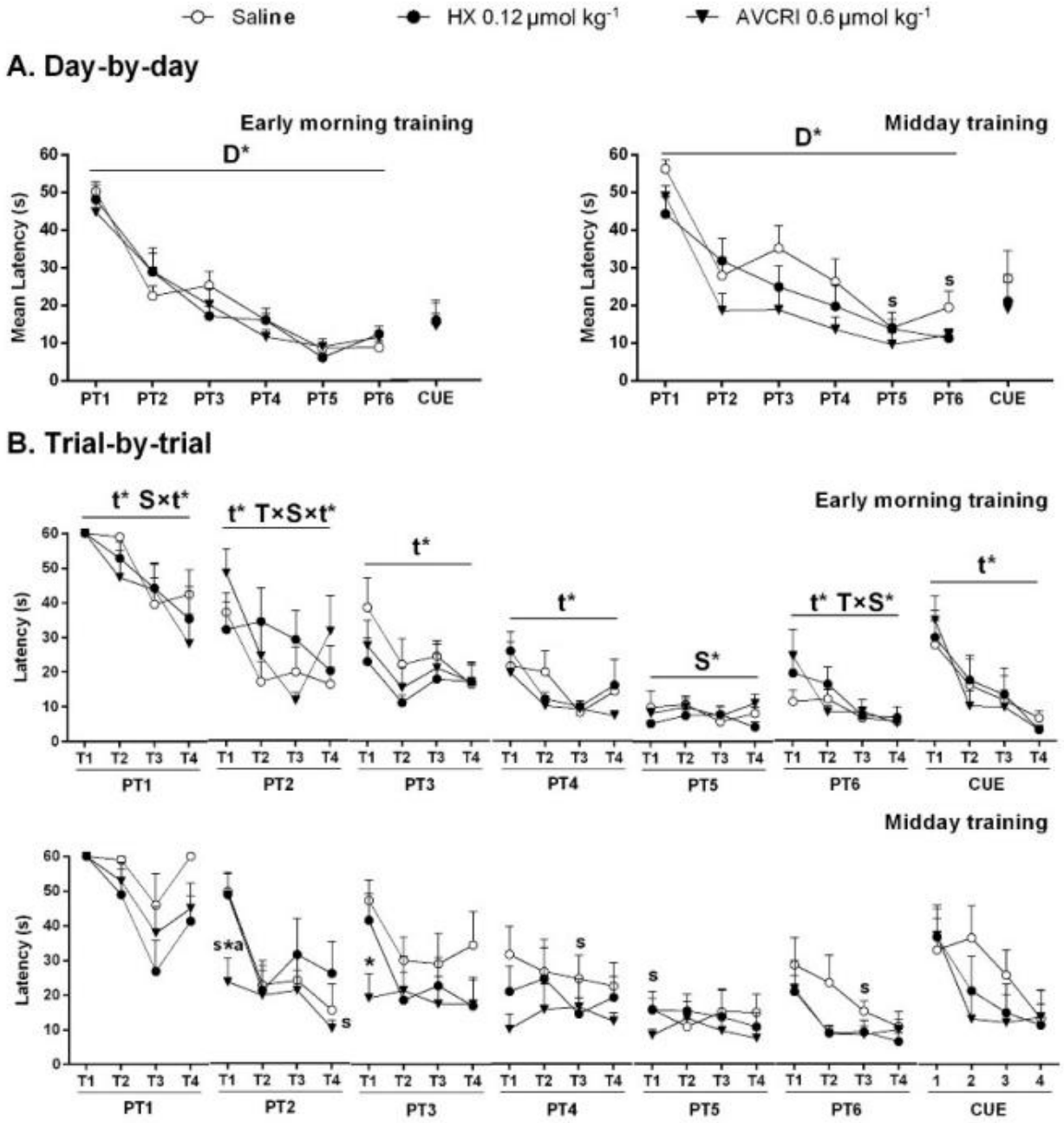












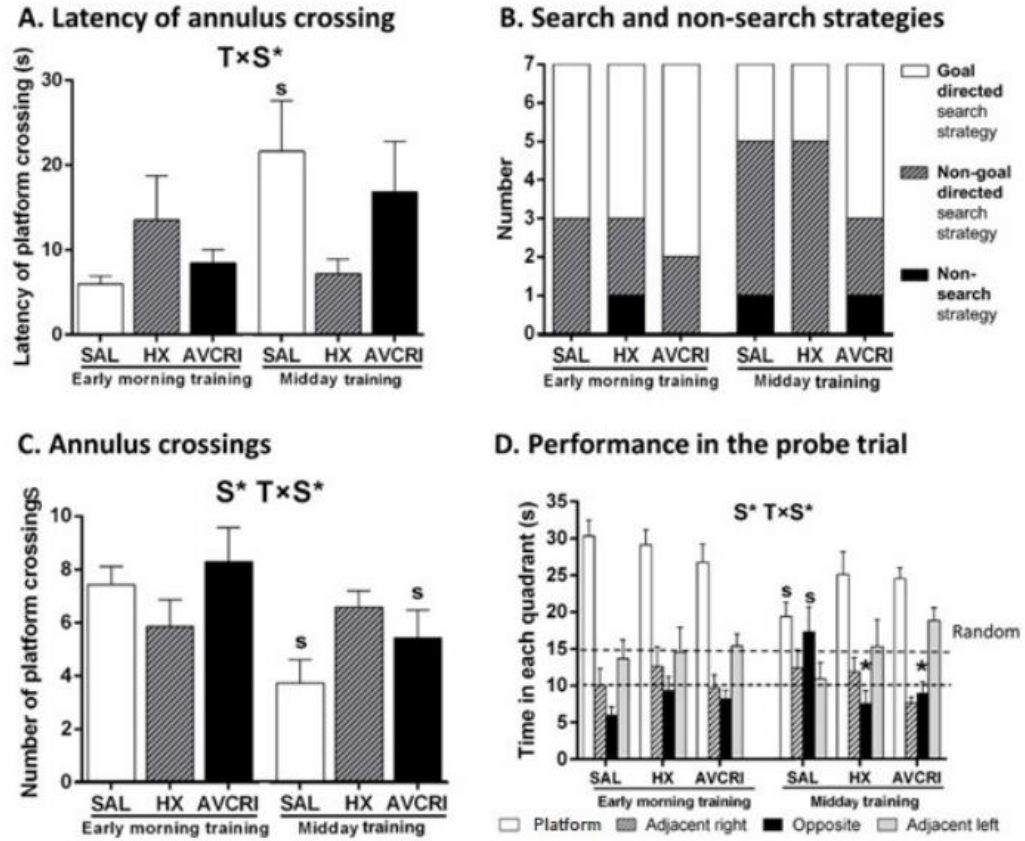
brain sciences

MDPI

Article

Clock/Sleep-Dependent Learning and Memory in Male 3xTg-AD Mice at Advanced Disease Stages and Extrinsic Effects of Huprine X and the Novel Multitarget Agent AVCRI104P3

Lydia Giménez-Llort [1,*], Mikel Santana-Santana [1], Míriam Ratia [2], Belén Pérez [2], Pelayo Camps [3], Diego Muñoz-Torrero [3], Albert Badia [2] and Maria Victòria Clos [2]

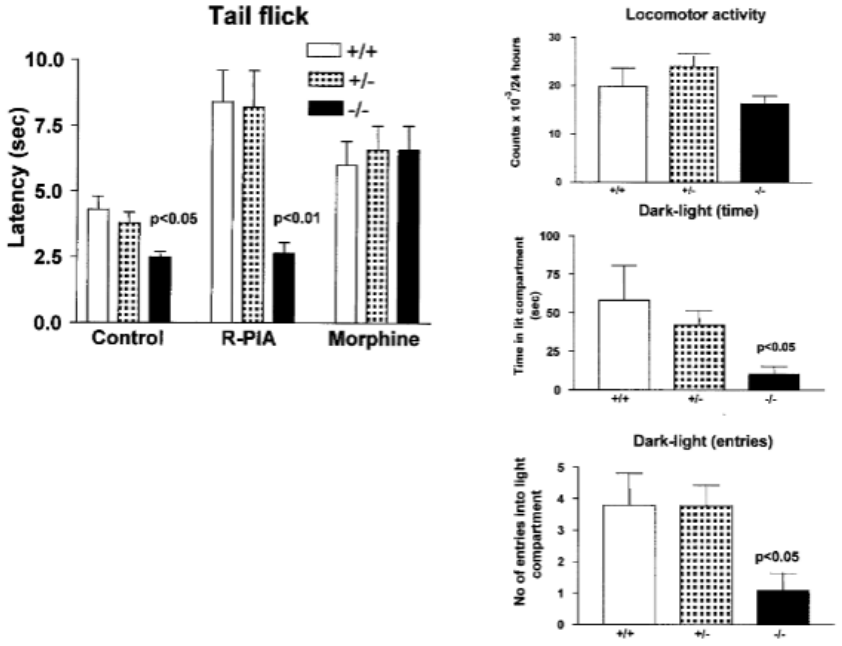


Hyperalgesia, anxiety, and decreased hypoxic neuroprotection in mice lacking the adenosine A_1 receptor

Björn Johansson*, Linda Halldner*, Thomas V. Dunwiddie†, Susan A. Masino‡, Wolfgang Poelchen†, Lydia Giménez-Llort‡, Rosa M. Escorihuela‡, Alberto Fernández-Teruel‡, Zsuzsanna Wiesenfeld-Hallin§, Xiao-Jun Xu§, Anna Hårdemark¶, Christer Betsholtz||, Eric Herlenius¶, and Bertil B. Fredholm*,**

*Department of Physiology and Pharmacology, Karolinska Institutet, S-171 77 Stockholm, Sweden; †Veterans Administration Medical Center and Department of Pharmacology, University of Colorado Health Sciences Center, Denver, CO 80262; ‡Department of Psychiatry and Forensic Medicine, School of Medicine, Autonomous University of Barcelona, E-08193 Bellaterra, Barcelona, Spain; §Departments of Medical Laboratory Sciences and Technology and ¶Women and Child Health, Karolinska Institutet, S-171 76 Stockholm, Sweden; and ||Department of Medical Biochemistry, University of Göteborg, S-405 30 Göteborg, Sweden

Communicated by Tomas Hökfelt, Karolinska Institute, Stockholm, Sweden, June 11, 2001 (received for review February 3, 2001)



EJN European Journal of Neuroscience
The official journal of FENS Federation of European Neuroscience Societies

Mice lacking the adenosine A_1 receptor are anxious and aggressive, but are normal learners with reduced muscle strength and survival rate

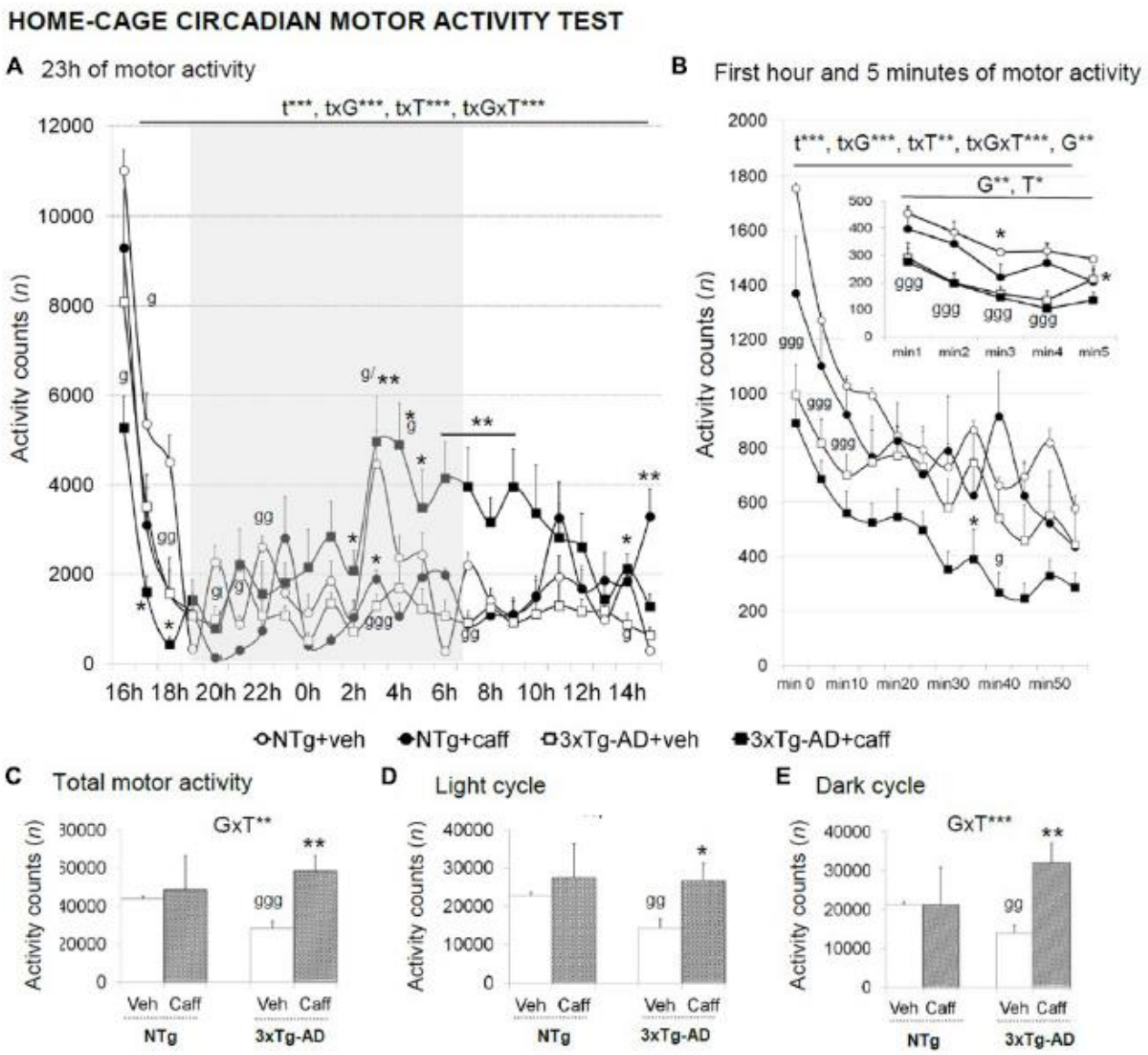
Lydia Giménez-Llort, Alberto Fernández-Teruel, Rosa Maria Escorihuela, Bertil B. Fredholm, Adolf Tobeña, Milos Pekny, Björn Johansson

First published: 23 August 2002 | https://doi.org/10.1046/j.1460-9568.2002.02122.x | Citations: 145

Long-term Treatment with Low-Dose Caffeine Worsens BPSD-Like Profile in 3xTg-AD Mice Model of Alzheimer's Disease and Affects Mice with Normal Aging

An exacerbation of BPSD-like symptoms may partly interfere with the beneficial cognitive effects of caffeine.

Front. Pharmacol.,15 Volume 9 - 2018 https://doi.org/10.3389/fphar.2018.00079

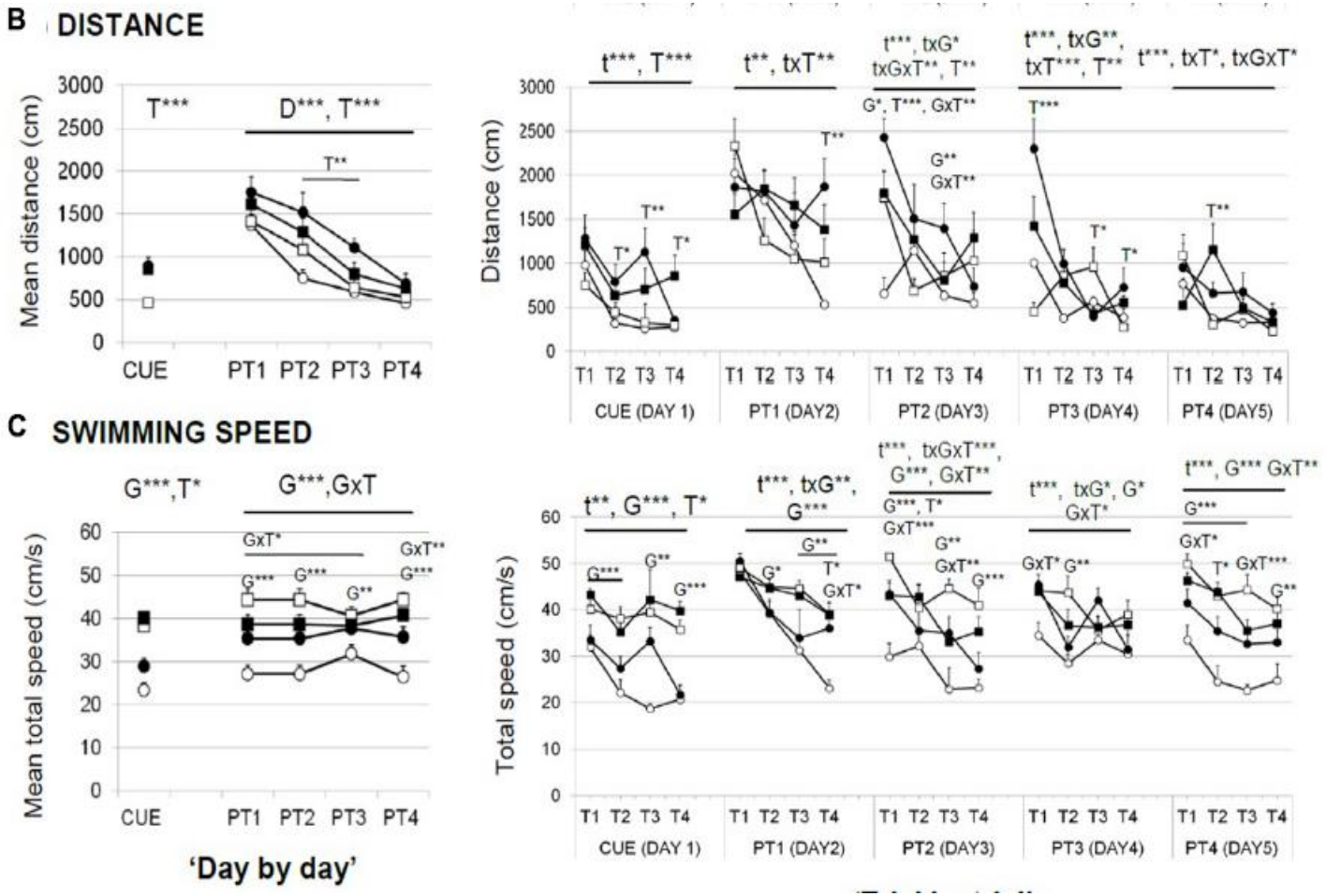


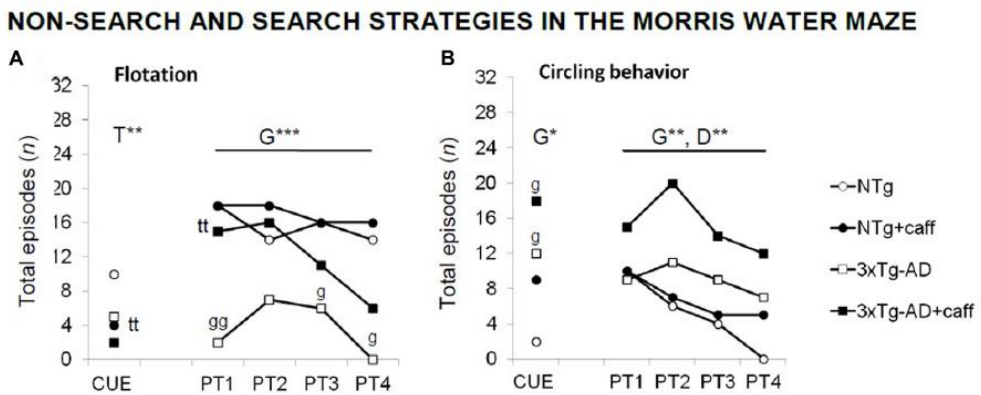
- **Significant effects on most behavioral variables**, especially those related to **neophobia and other anxiety-like behaviors**, **emotionality**, and **cognitive flexibility**.

- The 3xTg-AD and NTg mice were **differently influenced** by caffeine.

- Overall, the increase of neophobia and other anxiety-related behaviors resulted in an **exacerbation of BPSD-like profile in 3xTg-AD mice**.

- Circadian motor activity showed **genotype differences**, which were found to be **enhanced by caffeine.**





- **Learning and memory, strongly influenced by anxiety** in 3xTg-AD mice, **got little benefit from caffeine**, only shown after a detailed analysis of navigation strategies.
- The worsened pattern in NTg mice and the use of search strategies in 3xTg-AD mice make **both groups more similar**.
- Caffeine normalized **splenomegaly** of 3xTg-AD mice but increased **corticosterone** levels.

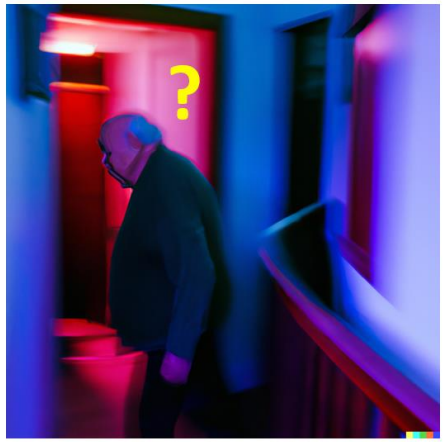
International Journal of *Molecular Sciences*

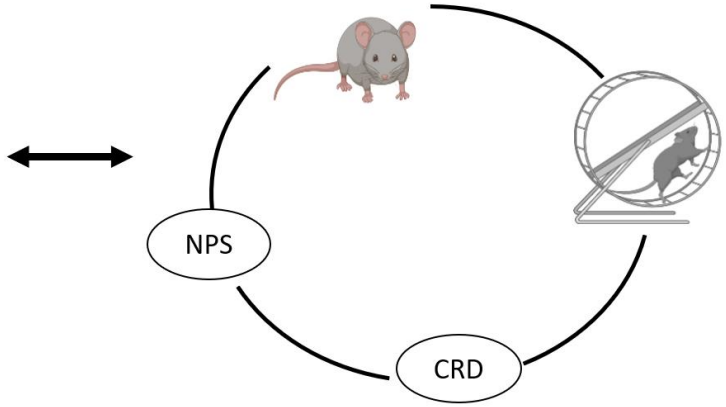
MDPI

Article

Sex- and Neuropsychiatric-Dependent Circadian Alterations in Daily Voluntary Physical Activity Engagement and Patterns in Aged 3xTg-AD Mice

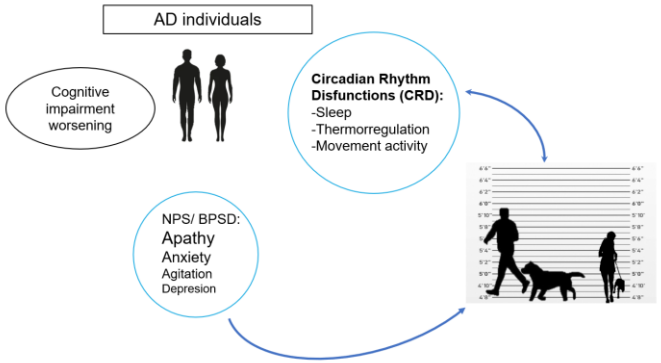
Daniel Alveal-Mellado [1,2], Lidia Castillo-Mariqueo [1,2] and Lydia Giménez-Llort [1,2,*]





Clinical setting

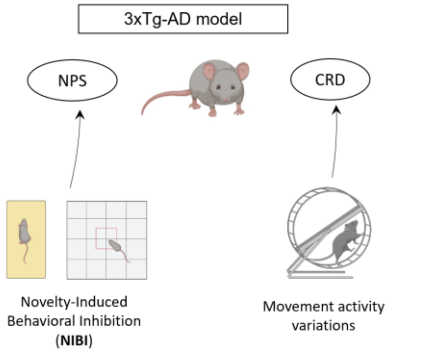
AD and Physical Activity (PA) levels



- **Physical Activity (PA) = non-structured physical exercise including activitites of daily living.** (Bowen et al., *Sport. Med.* **2011**, *41*, 73–86.)
- **Negative influence of NPS/BPSD on PA levels in AD patients.** (Watts., et al. PLoS One **2018**, 13)
- **Bidirectional relationship of CRD and PA levels in free living and institutionalized patients** (Nassan, M.; Videnovic, A. *Nat. Rev. Neurol.* **2022**, 18, 7–24)
- **Marked reduction of PA in older AD women patients.** (De Bono et al., Am. J. *Physiol. - Regul. Integr. Comp. Physiol.* **2006**, 290, 926–934)

Preclinical field

AD and Physical Activity (PA) levels



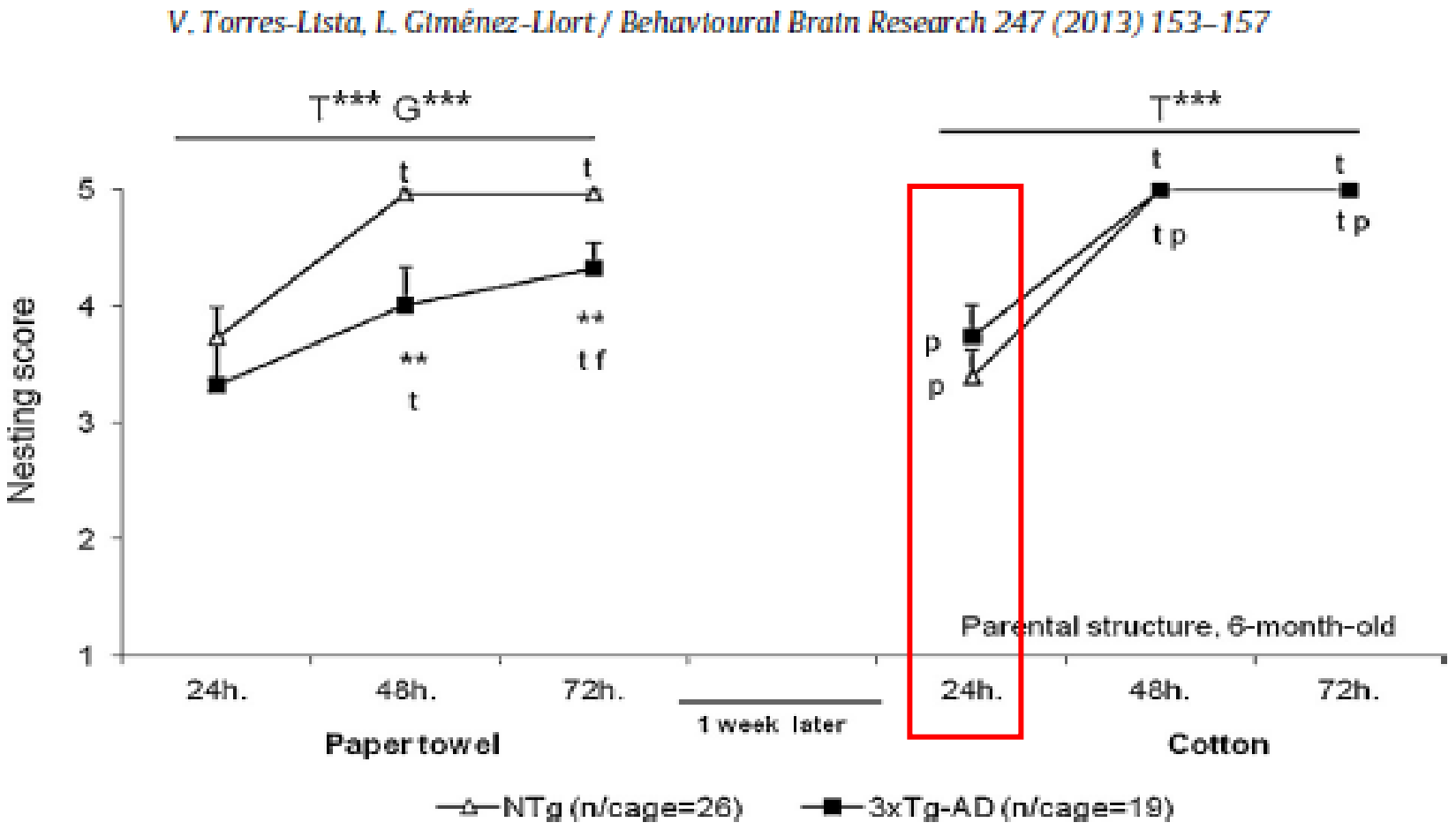
In 3xTg-AD

- **Good face and construct validity.** (Bilkei-Gorzo et al., *Pharmacol. Ther.* **2014**, 142, 244–57)
- **Replicates NPS symptoms.** (Giménez-Llort et al., *Neurosci. Biobehav. Rev.* **2007**, 31, 125–47)
- **Reproduces sleep and movement** activity disorder (Stover et al., *Behav. Brain Res.* **2015**, 289, 29–38)

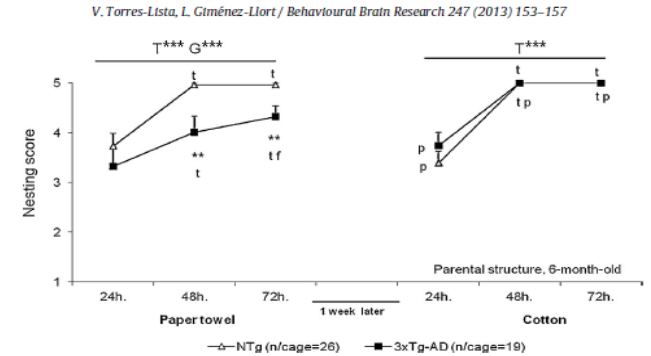
In NTg and other Tg models

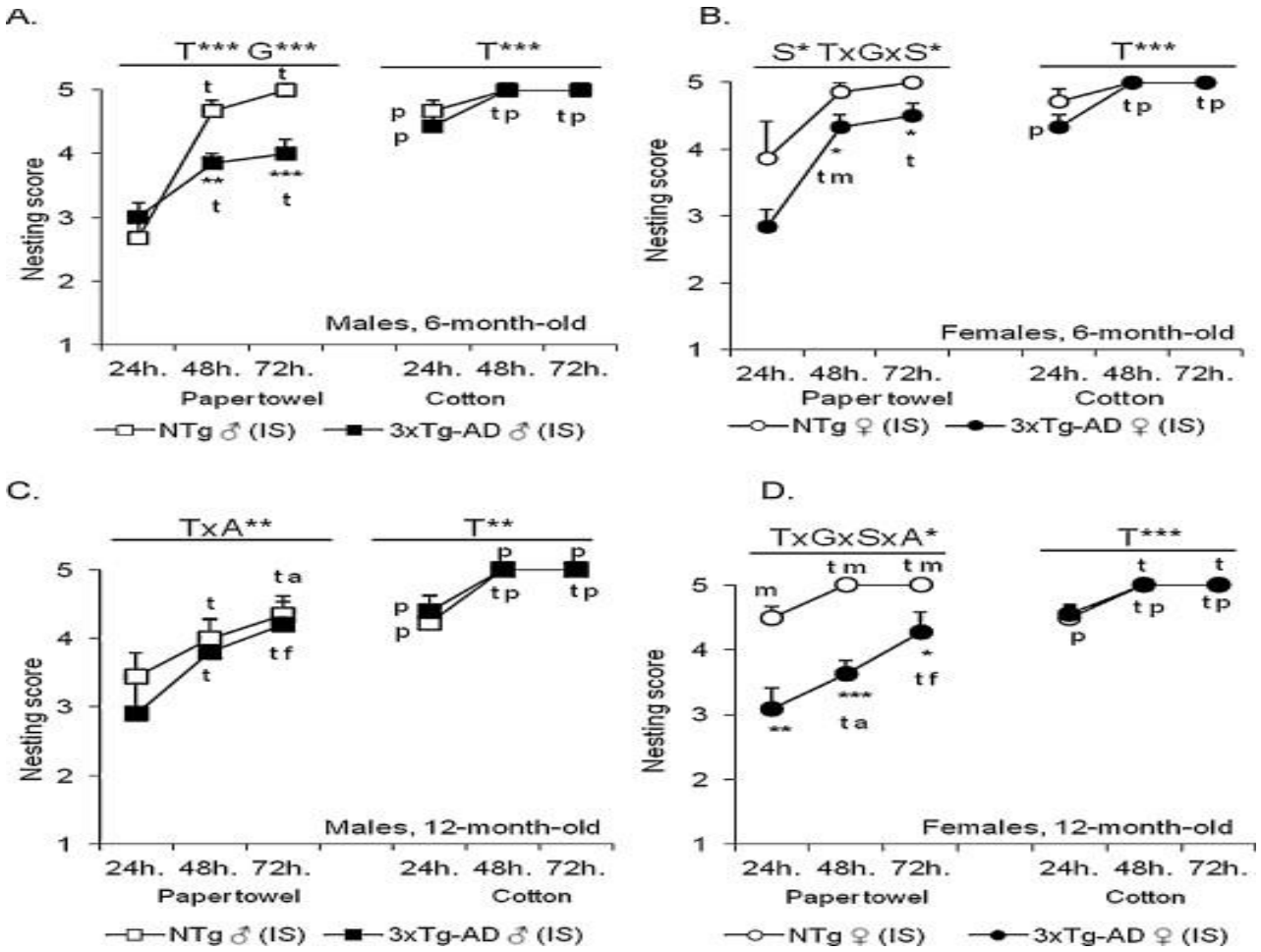
- **Age-dependent decline of activity in Running Wheel (RW)** (Ingram, D.K. *Med. Sci. Sports Exerc.* **2000**, 32, 1623–29)
- **Greater levels of PA in females.** (Bowen et al., *Sport. Med.* **2011**, 41, 73–86)

Nesting

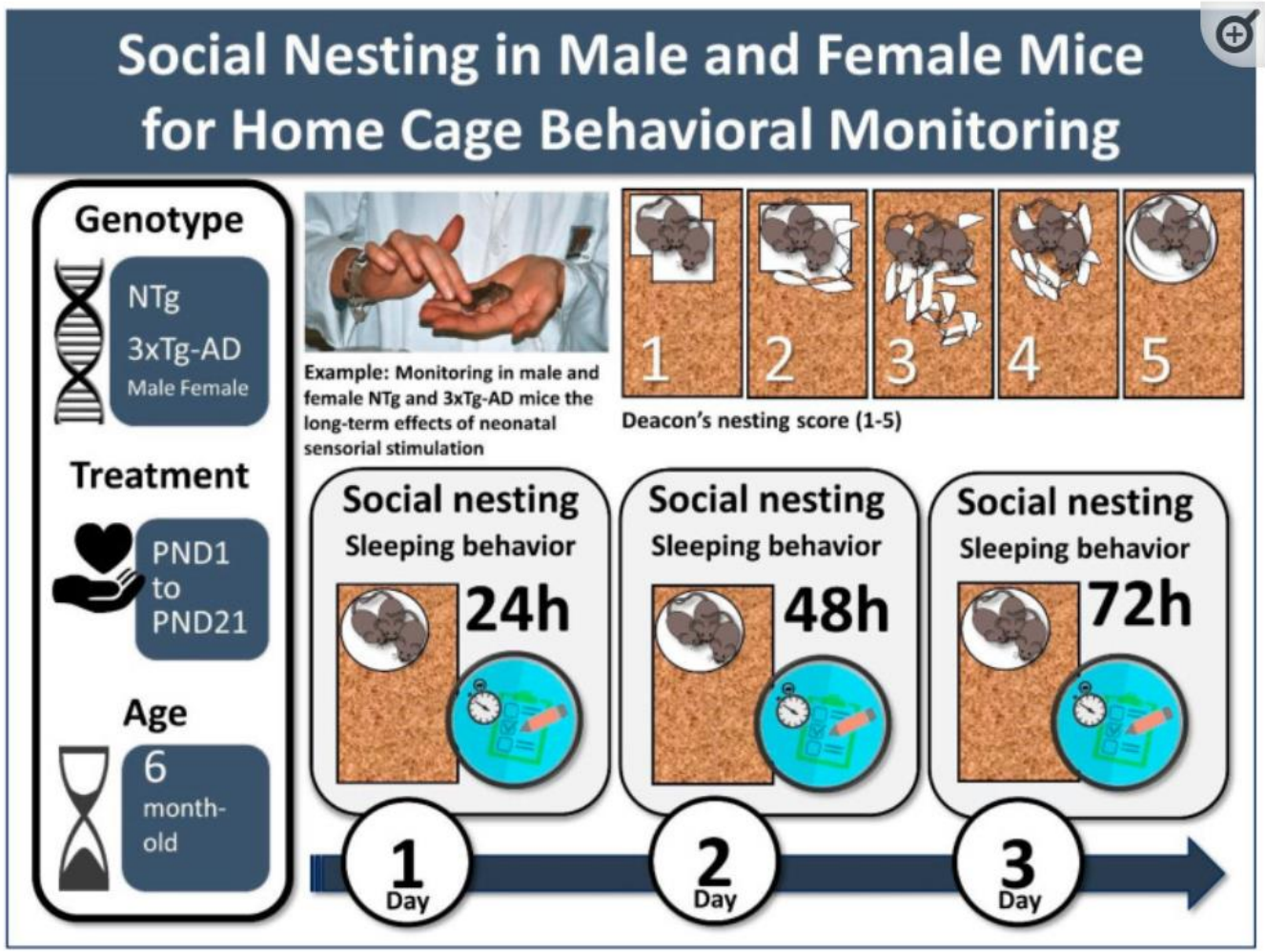


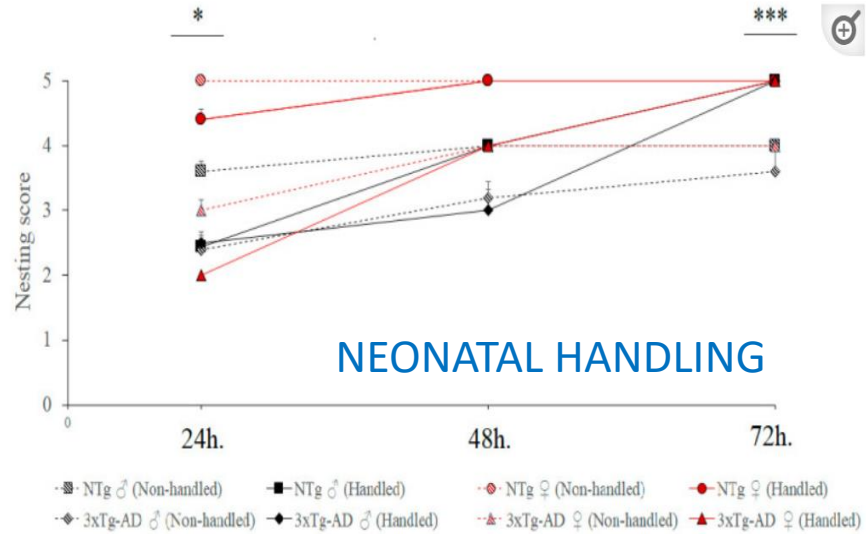
Deacon
Nesting Score
(Cotton, 24h, 1-5)





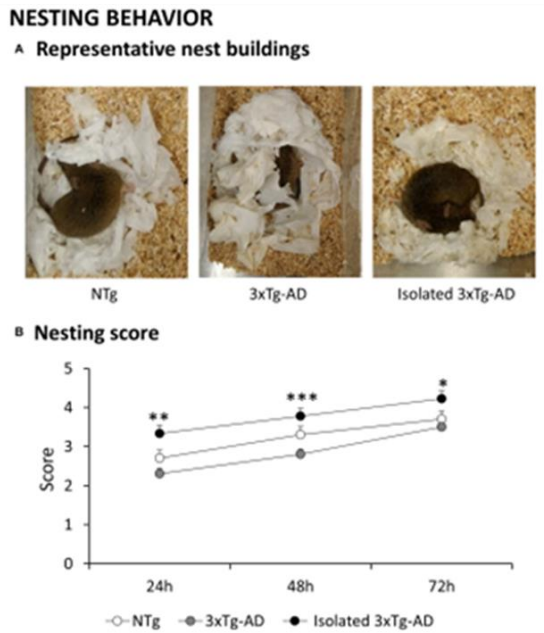
Nesting Behavior



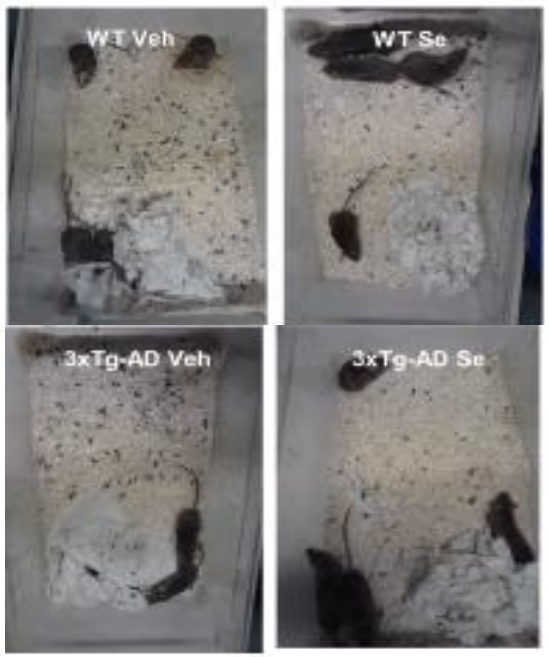


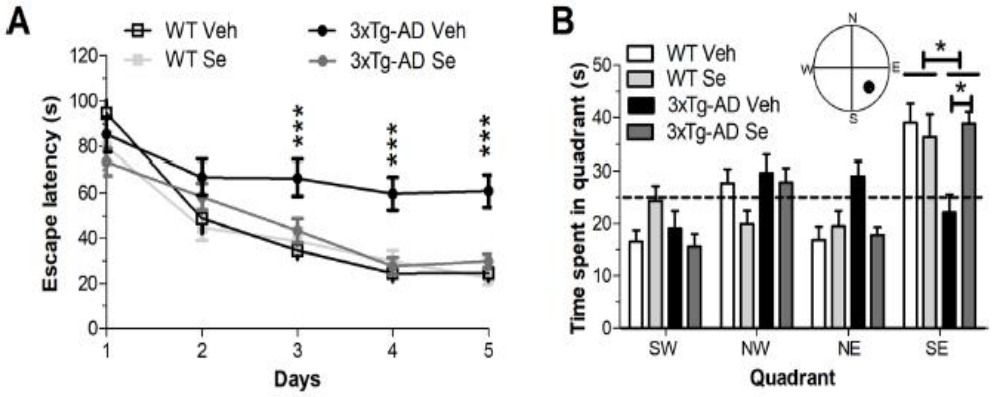
NEONATAL HANDLING

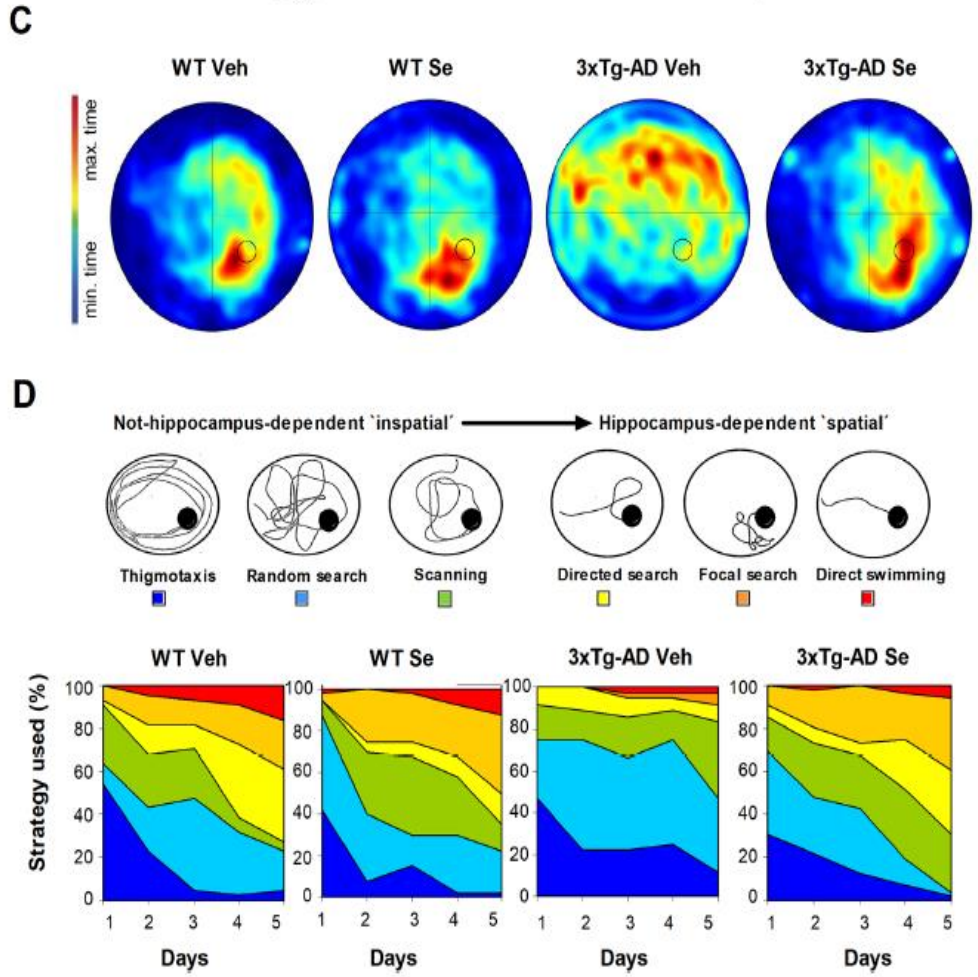
SOCIAL ISOLATION

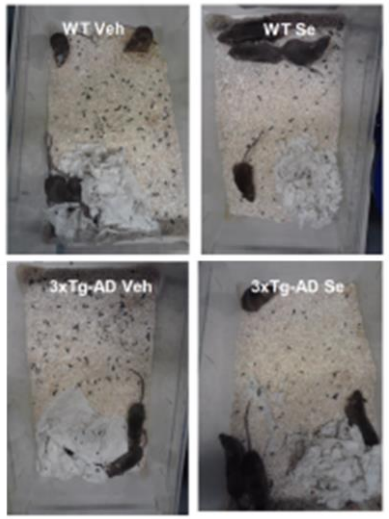


SELENIUM









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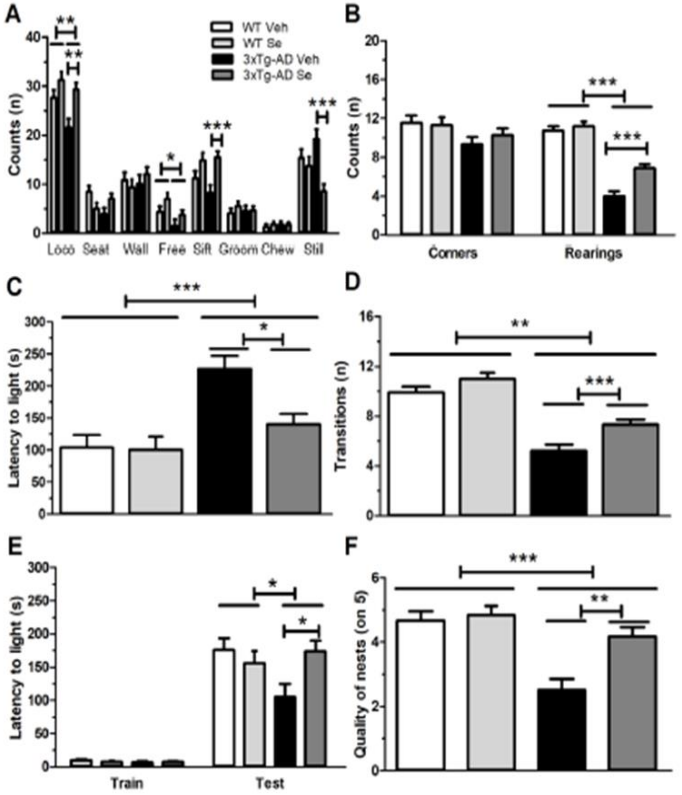
SCIENTIFIC REPORTS

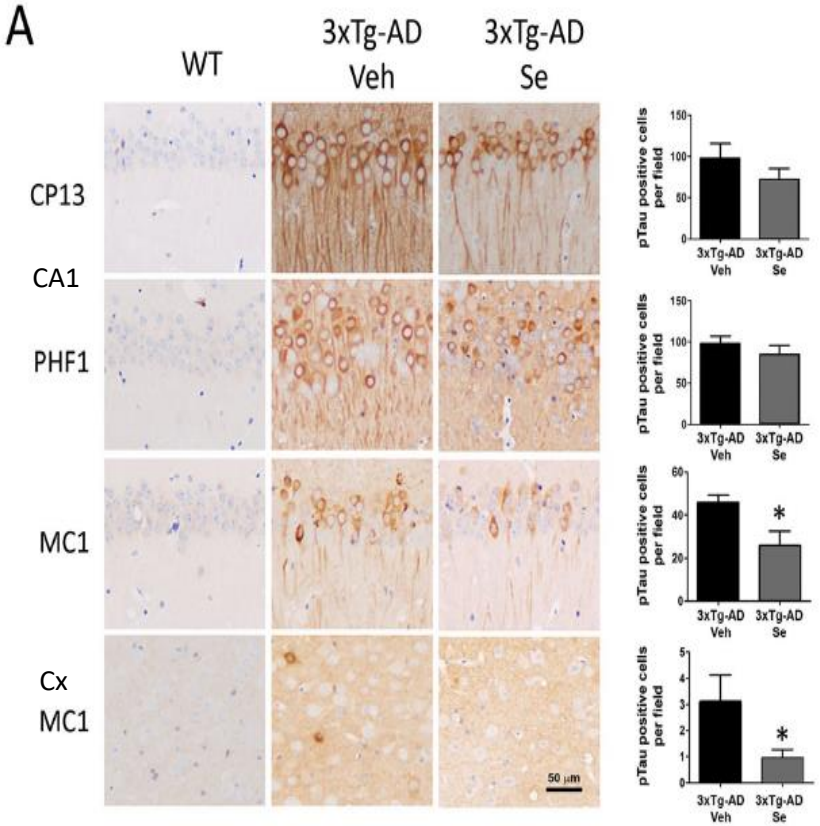
OPEN

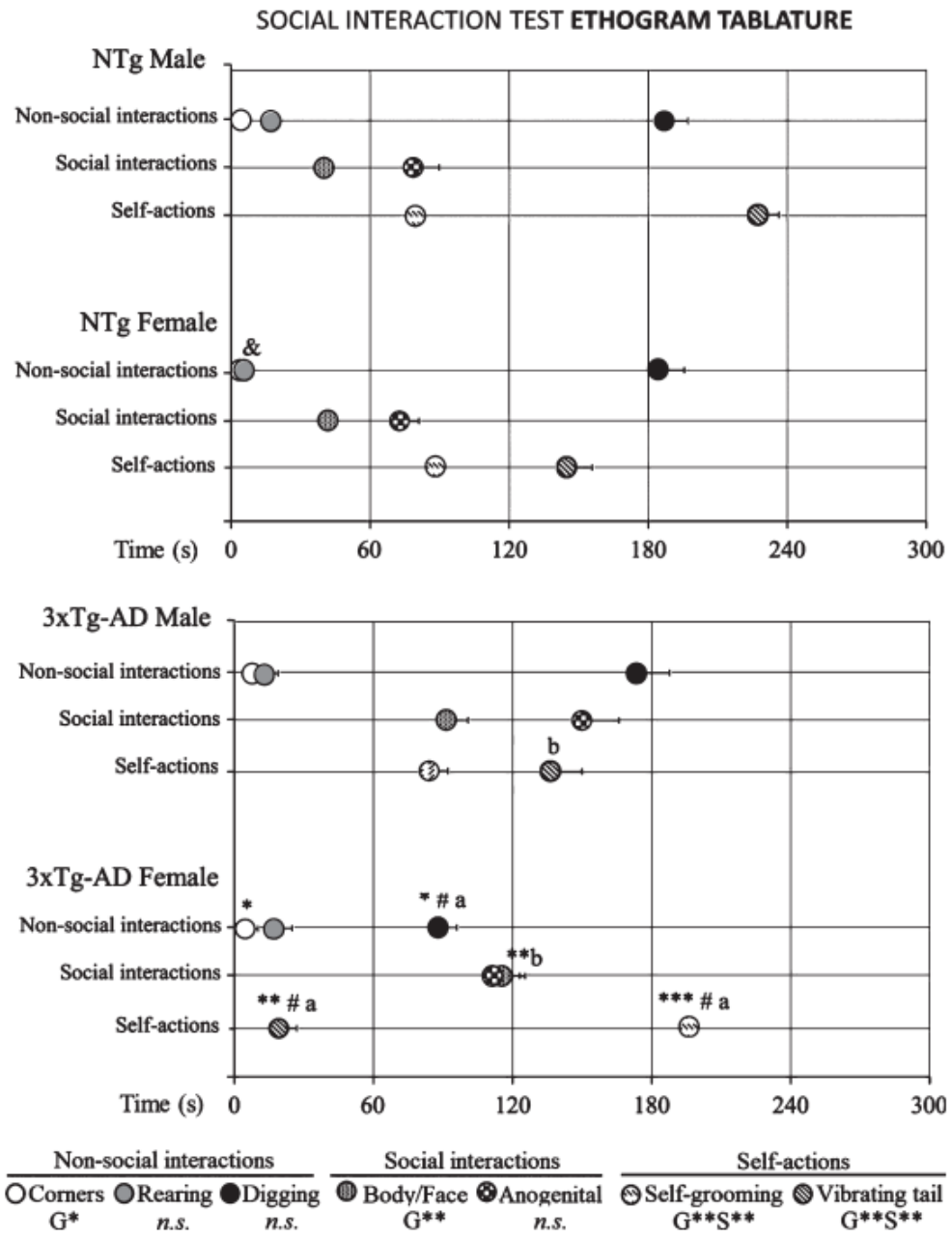
Reversal of memory and neuropsychiatric symptoms and reduced tau pathology by selenium in 3xTg-AD mice

Received: 25 January 2018
Accepted: 5 April 2018
Published online: 24 April 2018

Ann Van der Jeugd[1], Arnaldo Parra-Damas[2], Raquel Baeta-Corral[3], Carlos M. Soto-Faguás[2], Tariq Ahmed[1,5], Frank M. LaFerla[4], Lydia Giménez-Llort[3], Rudi D'Hooge[1] & Carlos A. Saura[2]







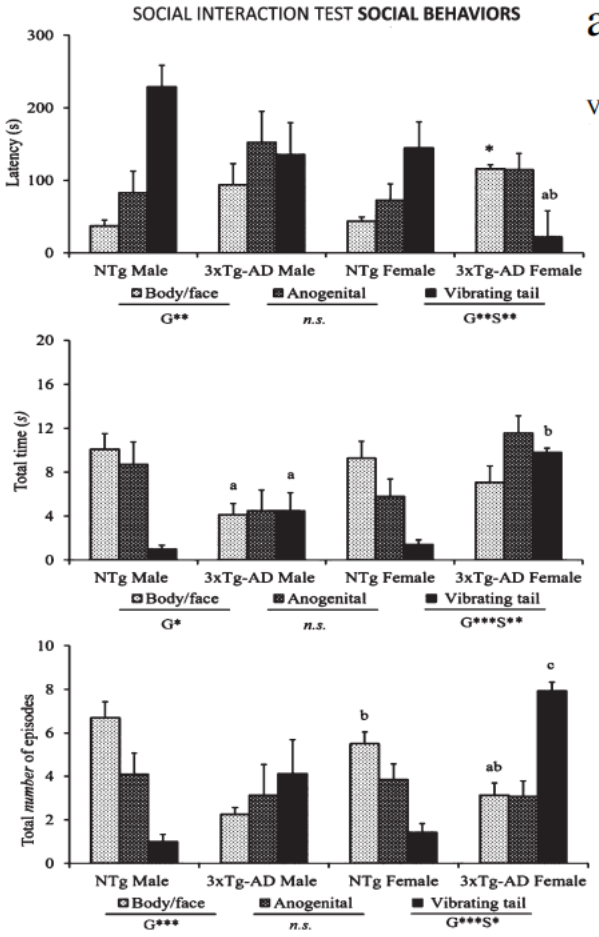
Brothers Sisters

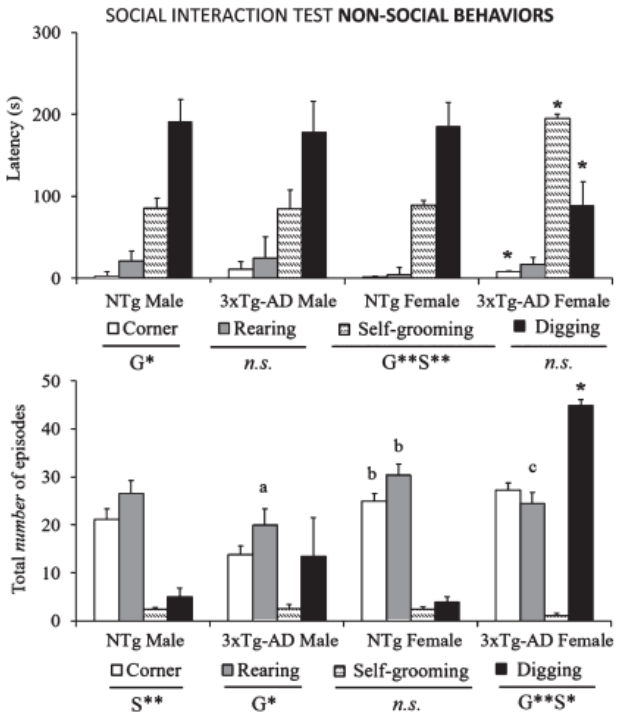
Journal of Alzheimer's Disease 69 (2019) 969–977
DOI 10.3233/JAD-190253
IOS Press

Short Communication

Vibrating Tail, Digging, Body/Face Interaction, and Lack of Barbering: Sex-Dependent Behavioral Signatures of Social Dysfunction in 3xTg-AD Mice as Compared to Mice with Normal Aging

Virginia Torres-Lista[a,b] and Lydia Giménez-Llort[a,b,*]





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Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Behavioural Brain Research 268 (2014) 185–201

Research report

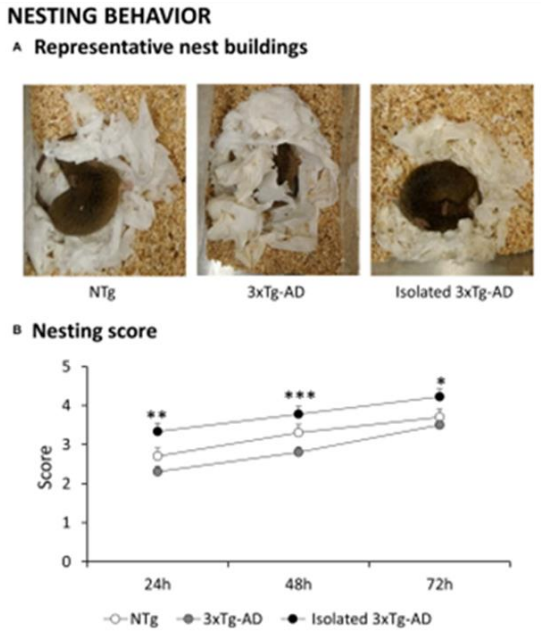
Cognitive and emotional profiles of aged Alzheimer's disease (3 × TgAD) mice: Effects of environmental enrichment and sexual dimorphism

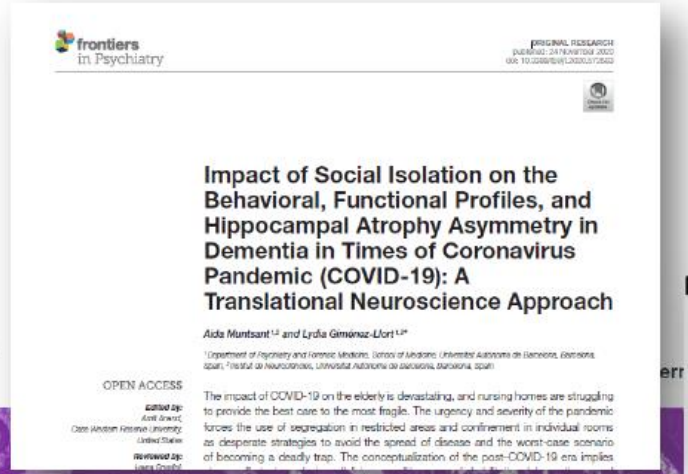
Gloria Blázquez *, Toni Cañete, Adolf Tobeña, Lydia Giménez-Llort, Alberto Fernández-Teruel

- Aged 3 × TgAD mice show deficits in spatial learning, short-term and working memory.
- 3 × TgAD mice show signs of increased anxiety and normal sensorimotor functions.
- Sexual dimorphism is reflected by increased behavioral inhibition in males.
- Sexual dimorphism is reflected by increased cognitive deficits in females.
- Environmental enrichment in adulthood induces beneficial effects on working memory.

Table 2
Behavioral battery results of 12- (A) and 15-month-old (B) NTg and 3 × TgAD, control and enriched (EE) male (left) and female (right) mice. Results are presented as mean ± standard error. G, T, indicate "genotype" or "treatment" effects. "Initial freezing": latency to the first movement. "Latency to white": latency to the first entry into the white compartment. "Entries into white": total number of entries in the white compartment. "Time in white": time spent in the white compartment.

(A) 12 months of age	Males						Females					
	NTg		3 × TgAD		F(1,36)	P≤	NTg		3 × TgAD		F(1,35)	P≤
	Control n = 11	EE n = 8	Control n = 11	EE n = 10			Control n = 10	EE n = 12	Control n = 10	EE n = 7		
Open field												
Initial freezing (s)	3.9 ± 1.4	7.5 ± 3.1	58.4 ± 25.9	21.5 ± 14.5	G 4.94	0.05	8.2 ± 2.2	12.7 ± 6.3	16.8 ± 4.5	5.7 ± 1.7	G 0.03	n.s.
Crossings	153.0 ± 20.3	116.1 ± 18.7	21.4 ± 12.8	48.9 ± 19.5	G 29.60	0.001	115.4 ± 12.2	76.1 ± 8.7	85.9 ± 19.4	78.4 ± 27.7	G 0.67	n.s.
Rearings	18.0 ± 3.7	12.5 ± 3.6	2.6 ± 1.3	2.7 ± 1.7	G 21.79	0.001	13.3 ± 2.6	7.8 ± 1.1	7.3 ± 2.2	7.3 ± 2.9	G 2.18	n.s.
Defecation boluses	2.0 ± 0.4	1.6 ± 0.3	2.9 ± 0.7	2.4 ± 0.4	G 2.64	n.s.	2.2 ± 0.7	1.3 ± 0.3	3.9 ± 0.4	4.4 ± 0.4	G 24.56	0.001
Dark–light box												
Latency to white (s)	48.2 ± 28.2	67.1 ± 38.4	165.7 ± 38.4	148.9 ± 41.5	G 7.08	0.05	82.6 ± 35.2	66.3 ± 31.9	113.7 ± 41.0	156.1 ± 51.0	G 2.37	n.s.
Entries into white	6.1 ± 1.3	5.5 ± 1.4	1.3 ± 0.5	1.8 ± 0.5	G 18.20	0.001	4.1 ± 0.9	3.1 ± 0.6	3.9 ± 1.1	2.1 ± 0.9	G 0.44	n.s.
Time in white (s)	82.1 ± 20.3	62.1 ± 17.9	13.7 ± 4.9	15.6 ± 5.1	G 18.25	0.001	52.0 ± 13.6	32.7 ± 7.2	59.3 ± 22.1	17.3 ± 8.4	G 0.08	n.s.
											T 4.43	0.05
Defecation boluses	3.1 ± 0.6	1.5 ± 0.6	3.8 ± 0.6	2.3 ± 0.6	G 1.39	n.s.	3.2 ± 0.5	1.8 ± 0.5	4.2 ± 0.5	4.0 ± 0.9	G 7.05	0.05
					T 6.18	0.05						
Hole board test												
Number of head-dips	21.0 ± 3.7	31.4 ± 8.1	19.4 ± 5.0	11.6 ± 3.2	G 4.28	0.05	19.7 ± 3.3	16.0 ± 2.9	23.7 ± 3.7	17.1 ± 3.8	G 0.51	n.s.
Time exploring (s)	17.0 ± 3.0	33.3 ± 9.9	16.1 ± 2.7	12.1 ± 2.9	G 4.12	0.052	18.2 ± 4.0	16.4 ± 3.7	54.2 ± 23.7	16.4 ± 3.8	G 1.25	n.s.
Defecation boluses	1.8 ± 0.4	2.1 ± 0.6	3.8 ± 0.8	3.1 ± 0.7	G 5.56	0.05	2.2 ± 0.6	1.7 ± 0.3	3.6 ± 0.9	3.4 ± 0.7	G 5.26	0.05
(B) 15 months of age												
Open field												
Initial freezing (s)	8.8 ± 3.2	4.1 ± 0.9	53.8 ± 22.8	38.0 ± 7.5	G 9.96	0.005	5.7 ± 1.4	3.7 ± 0.9	44.5 ± 17.0	35.1 ± 20.3	G 9.28	0.005
Crossings	64.0 ± 9.5	55.7 ± 13.6	63.7 ± 20.3	50.9 ± 16.6	G 0.02	n.s.	35.0 ± 5.1	44.3 ± 6.9	51.6 ± 11.3	48.3 ± 15.4	G 1.15	n.s.
Rearings	3.7 ± 1.3	4.5 ± 1.7	2.9 ± 1.6	0.7 ± 0.4	G 2.59	n.s.	1.6 ± 0.9	1.2 ± 0.7	1.5 ± 0.7	0.7 ± 0.7	G 0.13	n.s.
Defecation boluses	2.2 ± 0.7	3.9 ± 0.9	3.6 ± 0.8	3.4 ± 0.9	G 0.30	n.s.	3.0 ± 0.6	2.6 ± 0.4	3.5 ± 0.6	4.1 ± 1.2	G 2.35	n.s.





UAB Universitat Autònoma de Barcelona

Sala de premsa

Premsa i mitjans

Universitat Autònoma de Barcelona → Sala de premsa → Detall de noticia

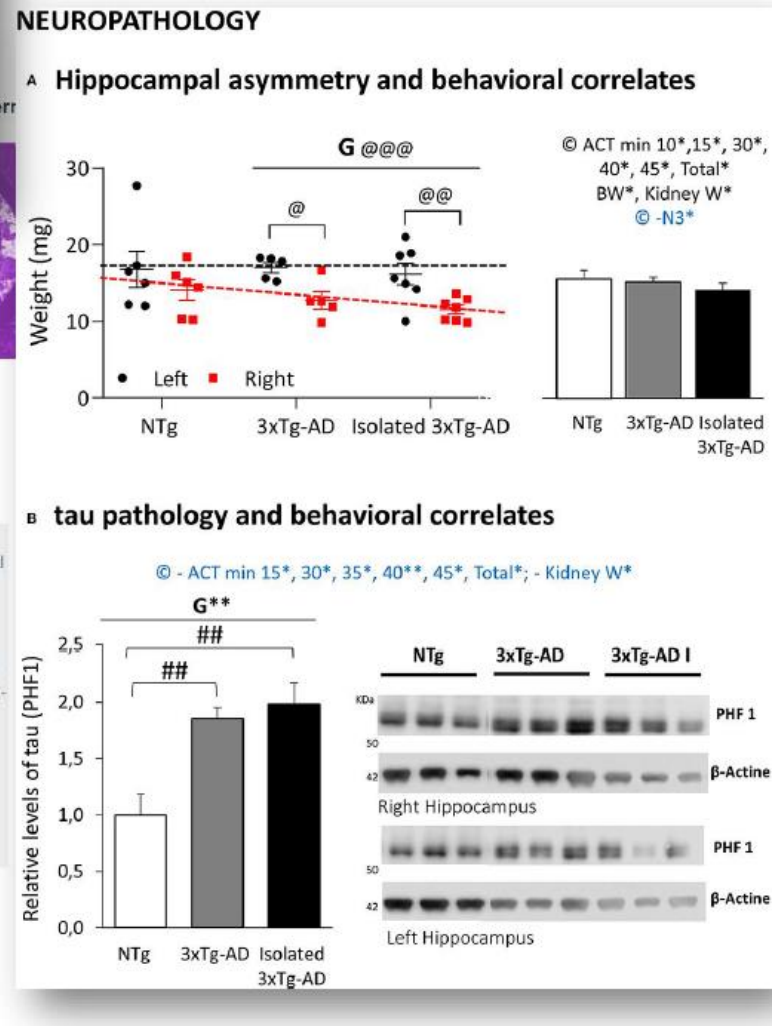
L'aïllament social augmenta l'agitació i l'asimetria en l'atròfia cerebral de la malaltia d'Alzheimer

Istock/Kiwis

Un estudi de la UAB mostra en ratolins que l'aïllament social agreuja la malaltia d'Alzheimer, augmentant fins al doble la hiperactivitat pròpia de la patologia, i constata un increment de l'asimetria de l'atròfia de l'hipocamp, una àrea cerebral clau per a la memòria. El treball s'ha publicat en un especial de *Frontiers in Psychiatry* sobre l'impacte de la mort, el dol i la solitud en temps de Covid-19.

01/10/2020

Investigadores del Departament de Psiquiatria i Medicina Legal i de l'Institut de Neurociències (INc) de la Universitat Autònoma de Barcelona (UAB) han dut a terme un estudi que permet estimar, des de la neurociència traslacional, l'impacte de l'aïllament dels escenaris actuals en temps de pandèmia en pacients



Food Finding Test: Sensorial behavioral paradigm for olfactory function in ageing neurodegeneration.

Daniela Marín-Pardo[1,2] and Lydia Gimenez-Llort[1,2]

Universidad de los Andes Colombia

Daniela Marin Pardo

Psychologist
MSc in Neuroscience
PhD Student in Neuroscience

UAB INc Institut de Neurociències

(Dziechciaz et al., 2014; Wilson et al., 2009; Volkers et al., 2011)

Sensory systems must ensure our ability to **perceive** and **recognize** the world

In older people **sensory deficiencies**

Have been proposed as **Predictors** of **cognitive decline**

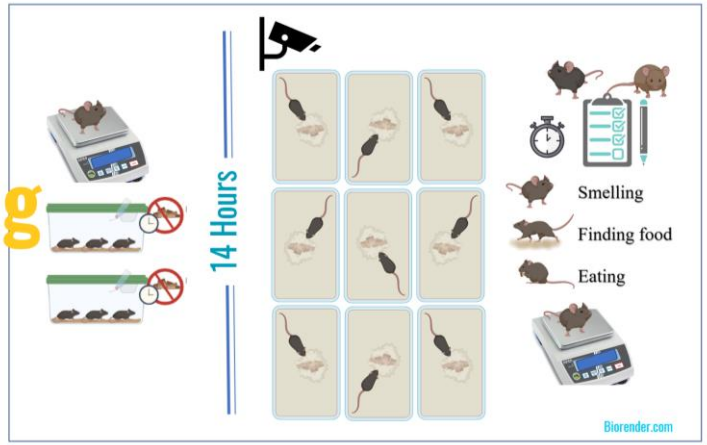
Early indicators of the prodromal stages of **Alzheimer's disease**

Olfactory impairment or deficiency may be an **indicator**

Increase their risk of **biological, psychological**, and **social impoverishment**

are more likely to Develop **Dementia**

Food Finding Test



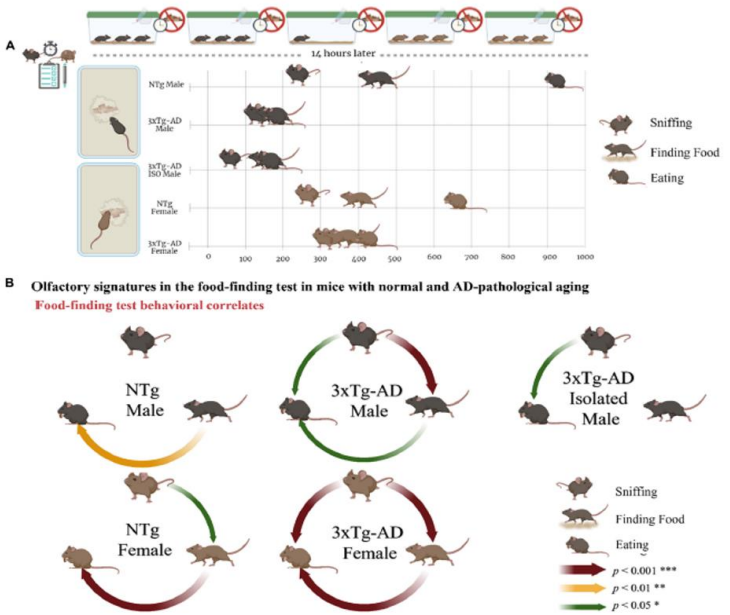
(Deacon et al., 2009)

Translational level

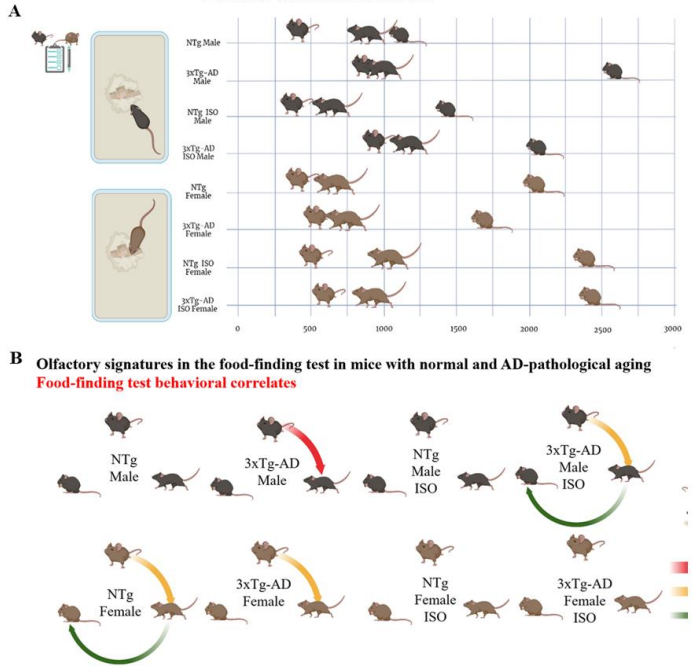
We have studied the olfactory signatures in male and female mice with n
associated with advanced stages of AD.

Olfactory Signatures in the Food Finding Test in Mice With Normal and Alzheimer's Disease-Pathological Aging With Special Concerns on the Effects of

Social Isolation



Forced Social Isolation



frontiers in Neuroscience

BRIEF RESEARCH REPORT
published: 05 October 2021
doi: 10.3389/fnins.2021.733984

Olfactory Signatures in the Food Finding Test in Mice With Normal and Alzheimer's Disease-Pathological Aging With Special Concerns on the Effects of Social Isolation

*Daniela Marin-Pardo[1,2] and Lydia Giménez-Llort[1,2]**

Neuroscience Letters
Volume 600, 23 July 2015, Pages 158-163

Research article

Tail-flick test response in 3×Tg-AD mice at early and advanced stages of disease

Raquel Baeta-Corral [a b], Ruti Defrin [c], Chagi G. Pick [d], Lydia Giménez-Llort [a b]

frontiers in Aging Neuroscience

BRIEF RESEARCH REPORT
published: 20 July 2021
doi: 10.3389/fnagi.2021.683412

Preserved Thermal Pain in 3xTg-AD Mice With Increased Sensory-Discriminative Pain Sensitivity in Females but Affective-Emotional Dimension in Males as Early Sex-Specific AD-Phenotype Biomarkers

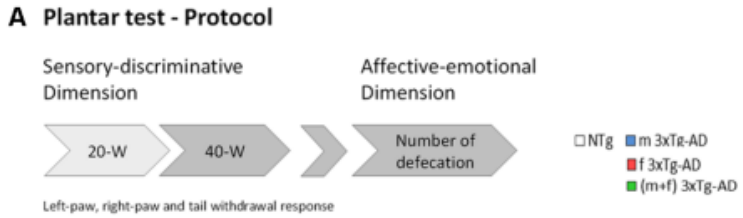
Toni Cañete [1,2] and Lydia Giménez-Llort [1,2]**

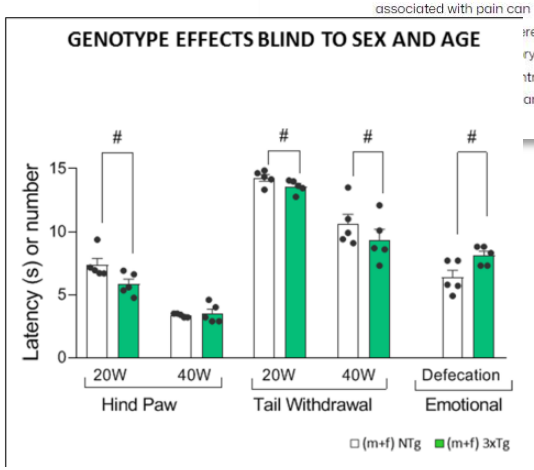
Sensitivity to painful external stimuli preserved in all phases of Alzheimer's disease in mice

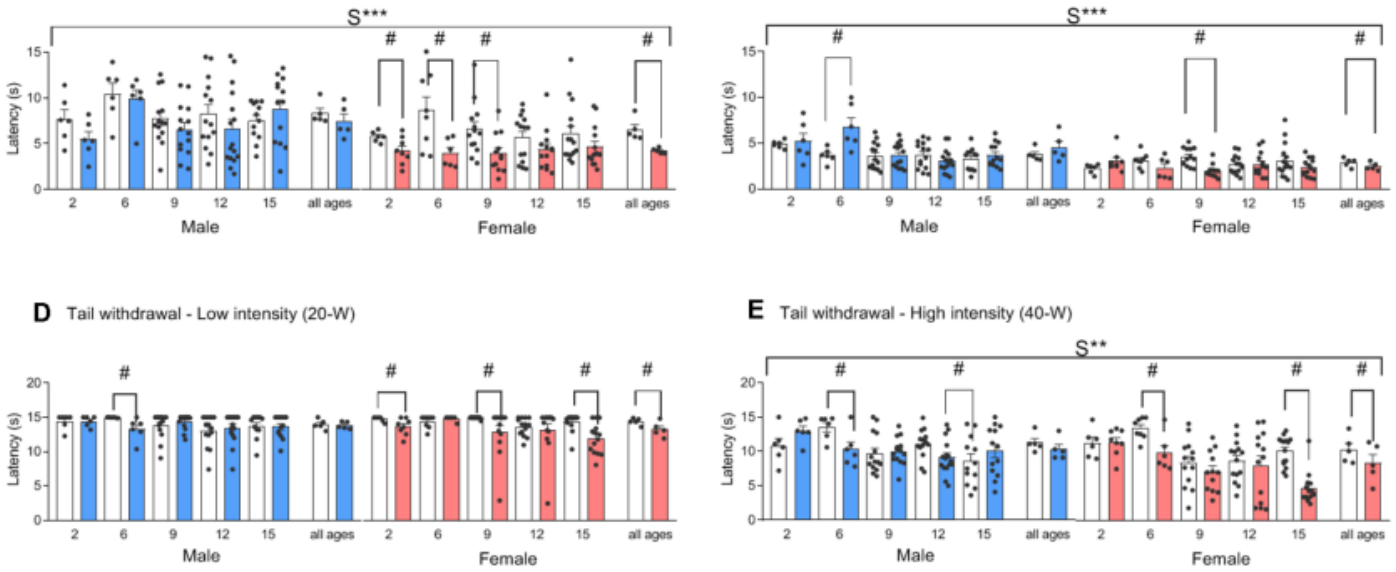
21 SEP 2021

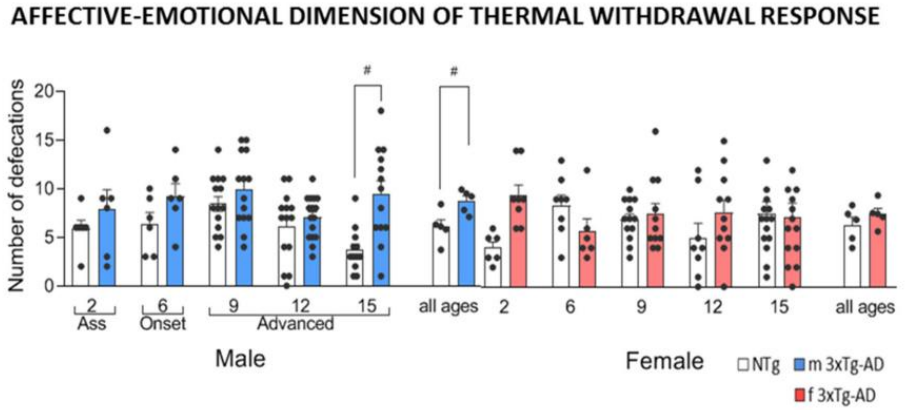
A UAB study in Alzheimer's disease in mice demonstrates that pain caused by a harmful external stimulus is preserved in all phases of the disease, even in the most advanced phases, and that there are differences in sensory and emotional reactions in males and females. The results validate the animal models used in the study of behaviours and mechanisms involved in the reaction to pain of people with dementia, as well as possible treatments.

The increase in number of people at very advanced ages, in which several chronic diseases associated with pain can









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Frank M. LaFerla, UCI

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