

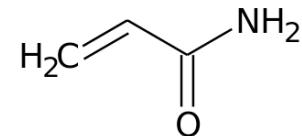
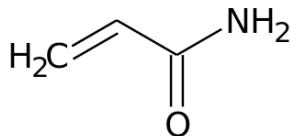
Project NATO-SFP-984777

# Acrylamide acute neurotoxicity in adult zebrafish

Demetrio Raldúa

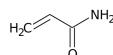


MINISTERIO  
DE CIENCIA, INNOVACIÓN  
Y UNIVERSIDADES



## Human acute acrylamide poisoning

- ✓ Occupational or accidental poisoning / *Suicide* attempts/ Intentional release



Toxic Industrial Chemical (TIC) → Terrorism



### Neurotoxicity



- ✓ MIE of ACR neurotoxicity is the **disruption of presynaptic vesicle cycling** by forming **adducts** with specific proteins: **synaptopathy**
- ✓ Decrease in the monoamine neurotransmitters content in rat brain has been reported



Depression and/or anxiety?

# Modelling human brain disorders in adult zebrafish

Review

Cell  
PRESS

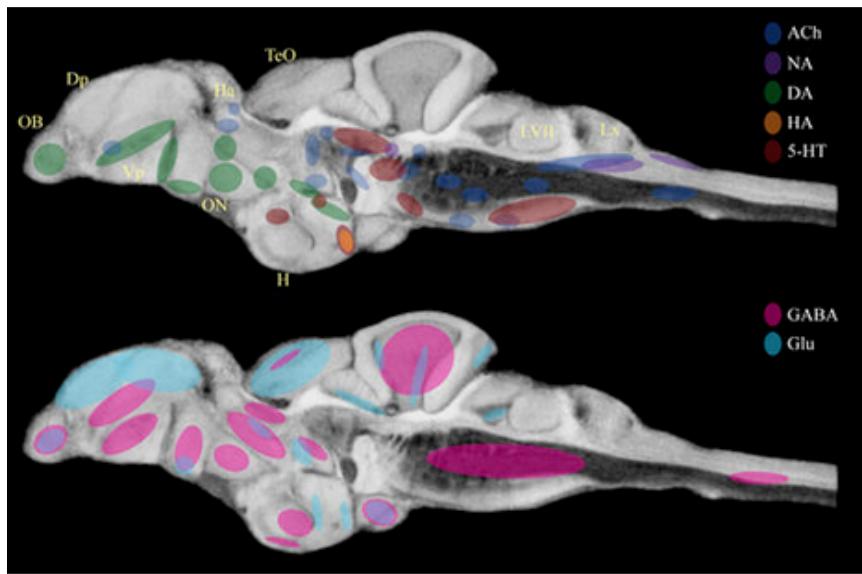
## Zebrafish as an emerging model for studying complex brain disorders

Allan V. Kalueff<sup>1</sup>, Adam Michael Stewart<sup>1,2</sup>, and Robert Gerlai<sup>3</sup>

<sup>1</sup> ZENEREI Institute and the International Zebrafish Neuroscience Research Consortium (ZNRC), 309 Palmer Court, Slidell, LA 70458, USA

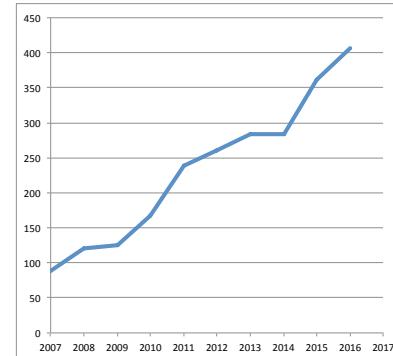
<sup>2</sup> Department of Neuroscience, University of Pittsburgh, A210 Langley Hall, Pittsburgh, PA 15260, USA

<sup>3</sup> Department of Psychology, University of Toronto at Mississauga, 3359 Mississauga Road North, Mississauga, Ontario L5L 1C6, Canada

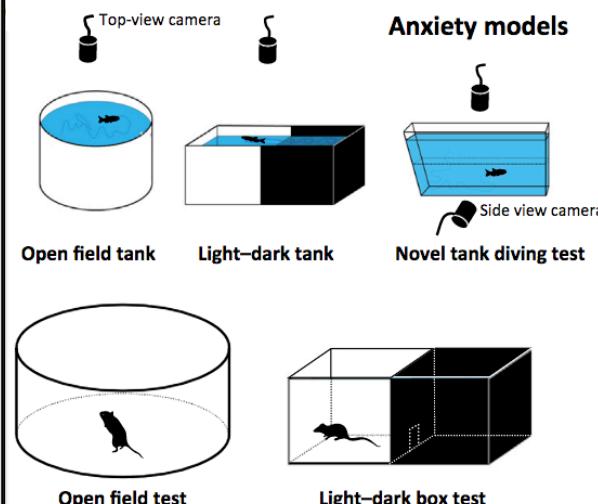
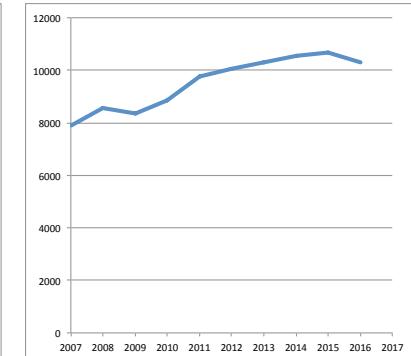


Pubmed: 2007-2016 (10 years)

zebrafish AND behavior



rodents AND behavior



# **Objective**

**To determine if acute exposure to ACR induces  
anxiety and/or depression**

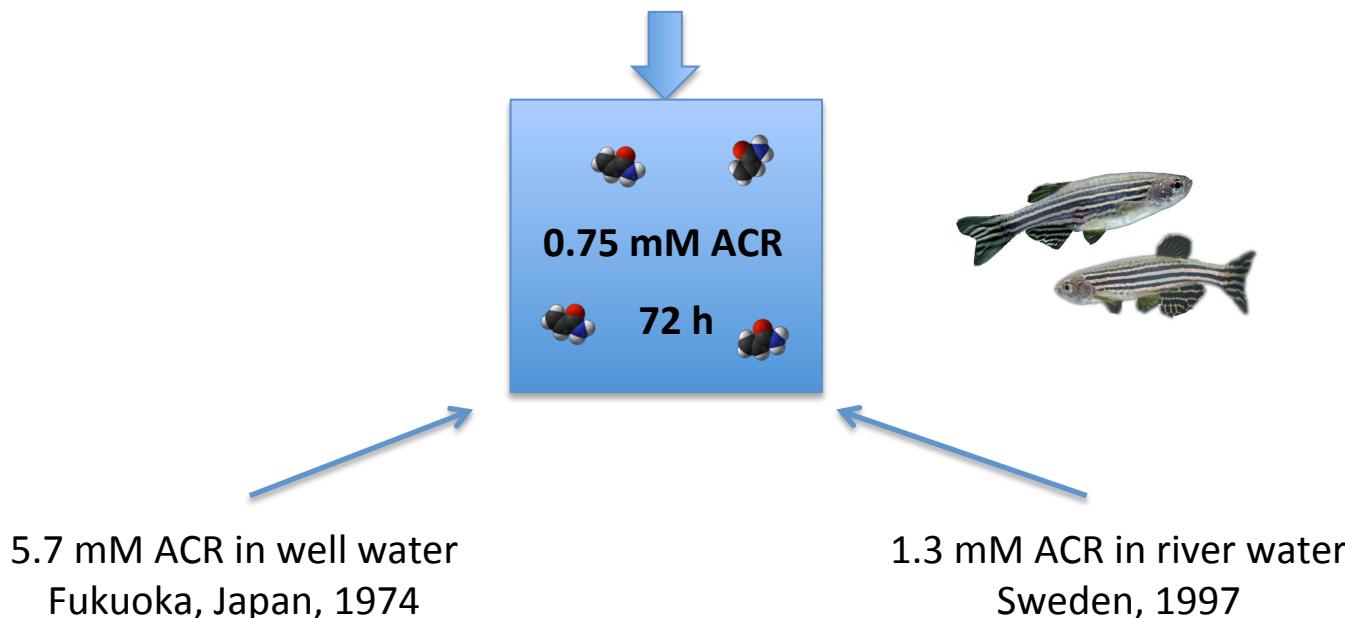
# SCIENTIFIC REPORTS

OPEN

## Acrylamide acute neurotoxicity in adult zebrafish

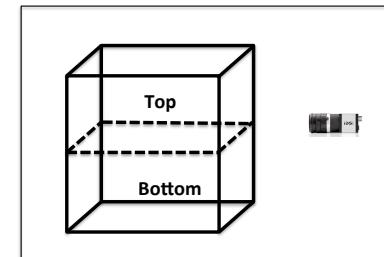
Received: 7 March 2018

Melissa Faria<sup>①</sup>, Tamar Ziv<sup>②</sup>, Cristian Gómez-Canela<sup>③</sup>, Shani Ben-Lulu<sup>②</sup>, Eva Prats<sup>③</sup>, Karen Adriana Novoa-Luna<sup>④</sup>, Arie Admon<sup>②</sup>, Benjamin Piña<sup>①</sup>, Romà Tauler<sup>①</sup>, Leobardo Manuel Gómez-Oliván<sup>④</sup> & Demetrio Raldúa<sup>②</sup><sup>1</sup>

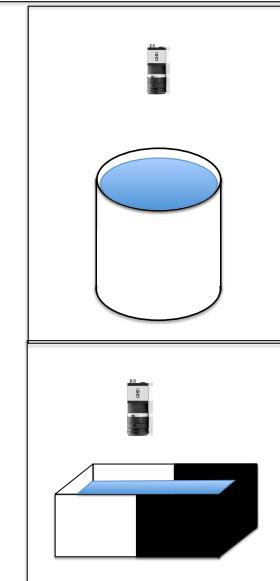


## ✓ Behavioral analysis

1. Novel Tank Test (NTT) → **geotaxis**



2. Open Field Test (OFT) → **thigmotaxis**



3. Dark-Light Test (LDT) → **scototaxis**

4. Shoaling → **social cohesion**

Cortisol levels/ Skin coloration



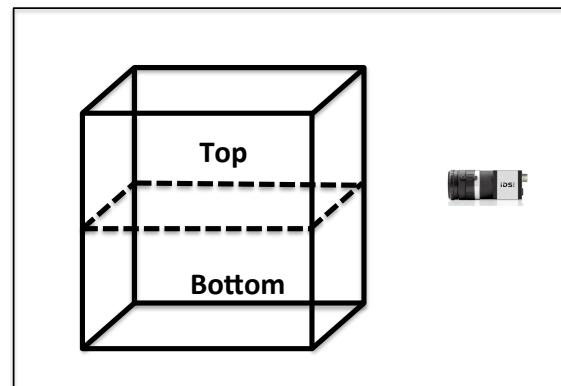
## ✓ Neurotransmitters profile:

LC-MS/MS

38 metabolites

# Effects on behavior

## Novel Tank Test



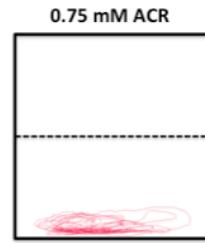
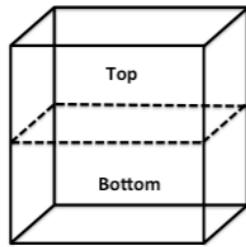
- ✓ Total distance
- ✓ Distance moved in each zone
- ✓ Time spent in each zone
- ✓ **Latency to enter the top zone**
- ✓ Number of transitions to top zone

- ✓ Freezing
- ✓ Erratic movements

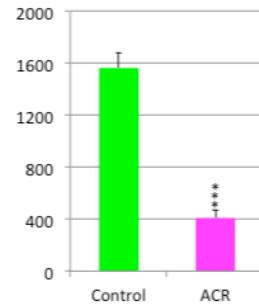


Anxiety/fear hallmarks

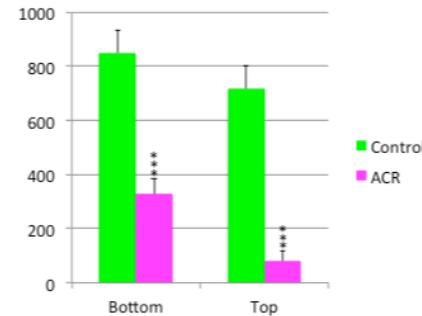
# Hypolocomotion/ Positive geotaxis



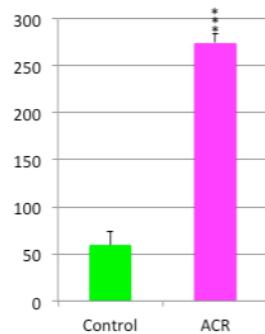
Total distance  
(cm)



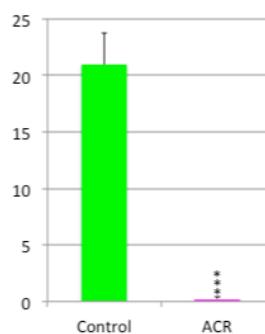
Distance (cm):  
Bottom vs Top



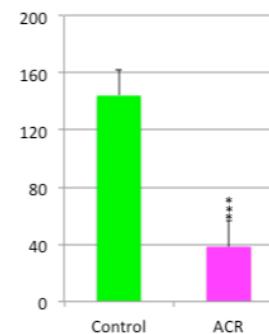
Latency to top (s)

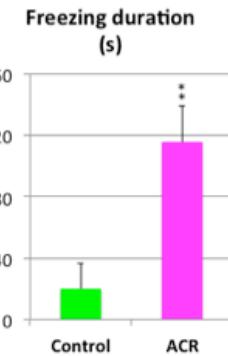
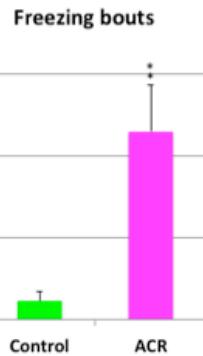
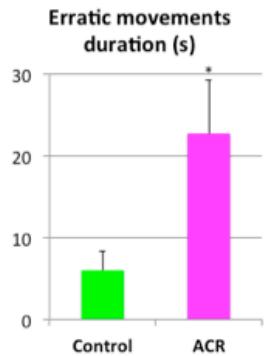


Transitions to top

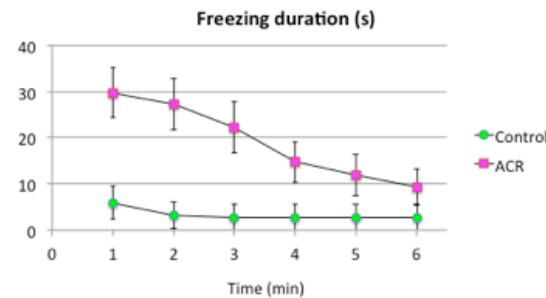
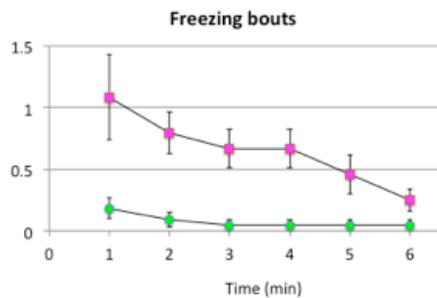


Time (s) in the top

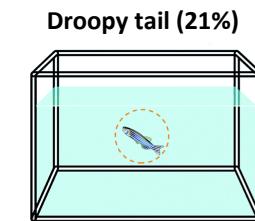
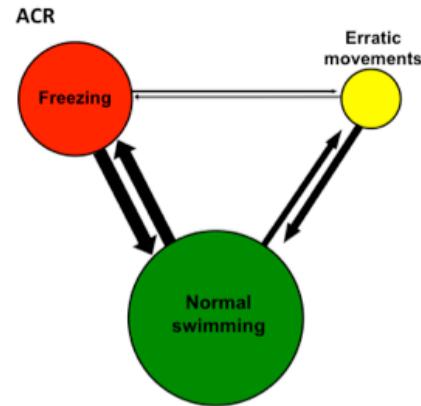
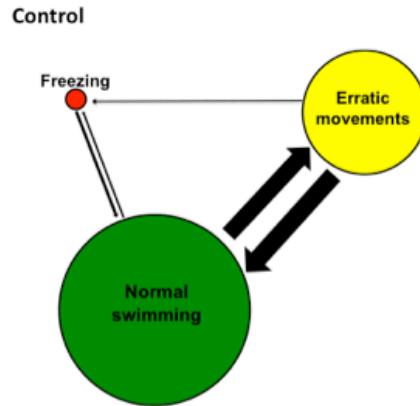




↑ **Freezing**

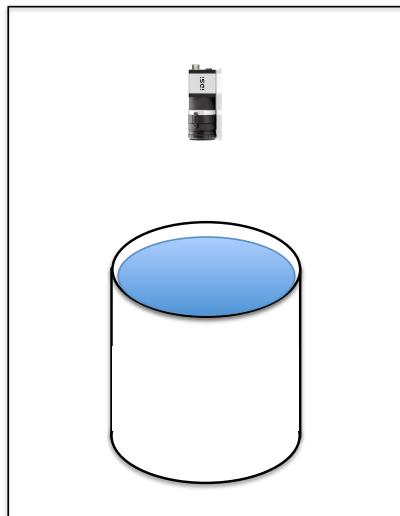


↑ **Erratic movements**



# Effects on behavior

## Open Field Test



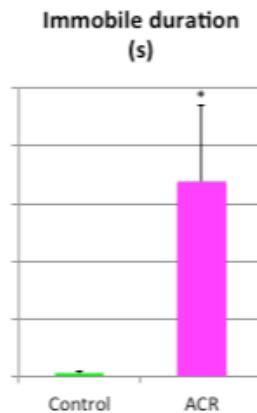
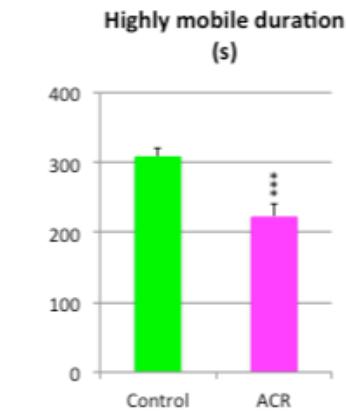
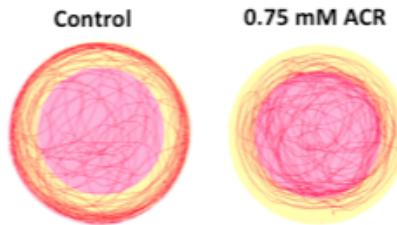
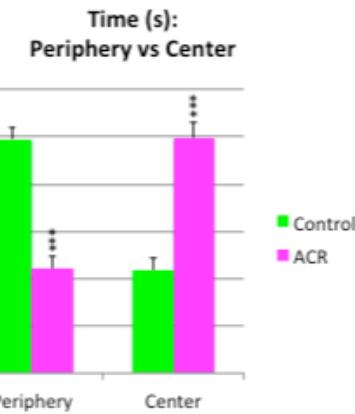
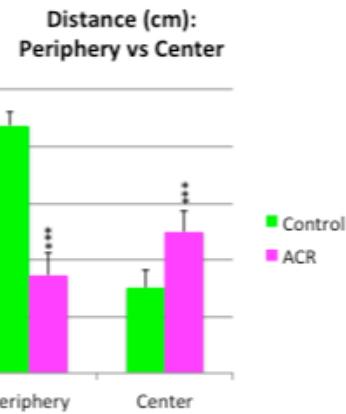
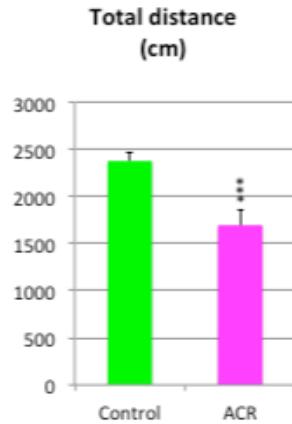
- ✓ Total distance
- ✓ Distance moved in center/periphery
- ✓ Time spent in center/periphery
- ✓ Mobility states

- ✓ Turn angle
- ✓ Angular velocity
- ✓ Meandering
- ✓ Tight circling

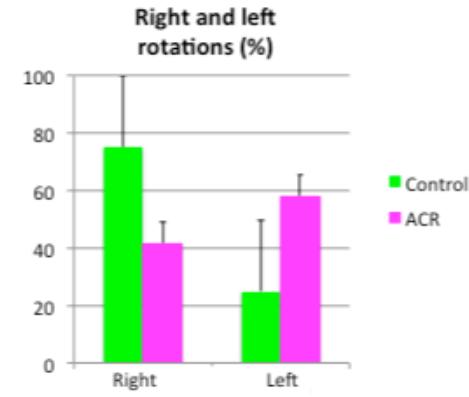
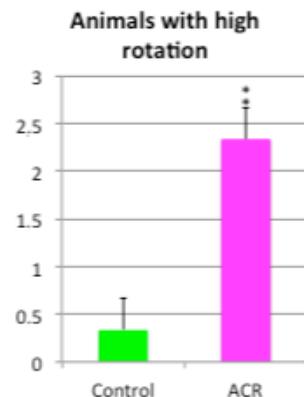
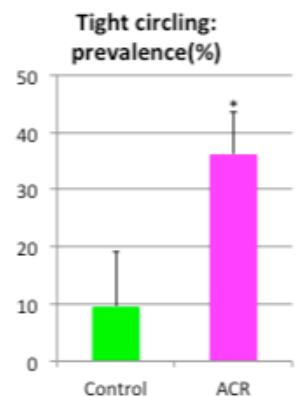
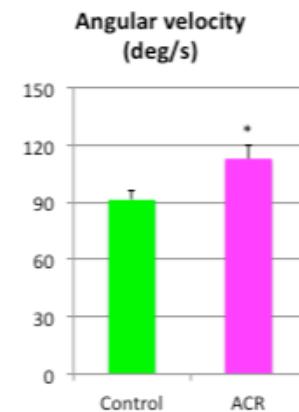
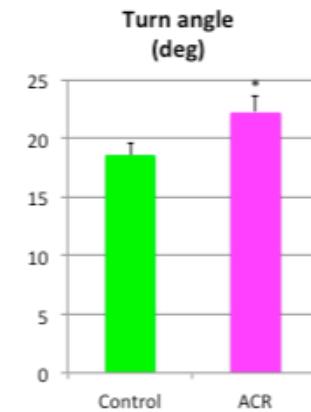
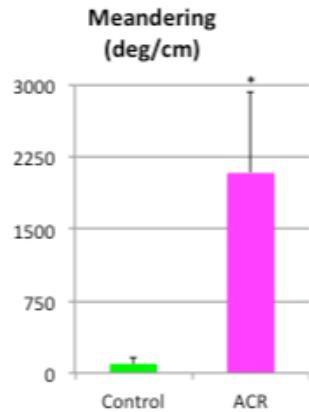


Changes in moving direction

# Hypolocomotion/ Negative thigmotaxis

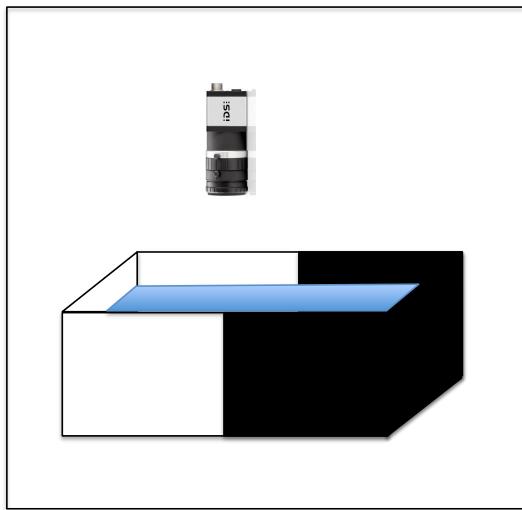


# Increased angular movement/ Tight circling



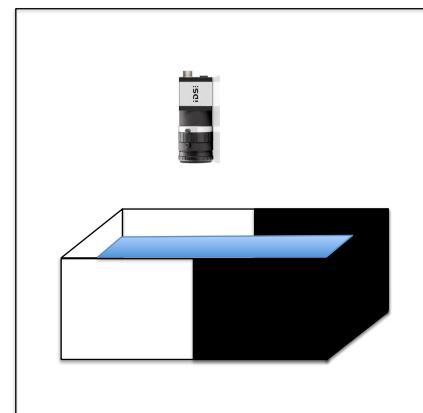
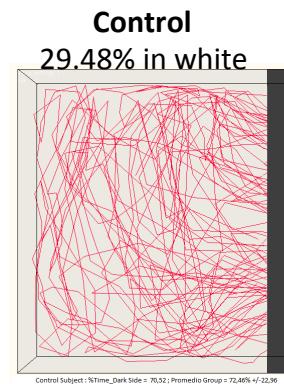
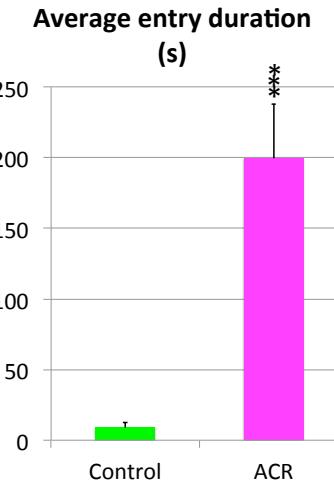
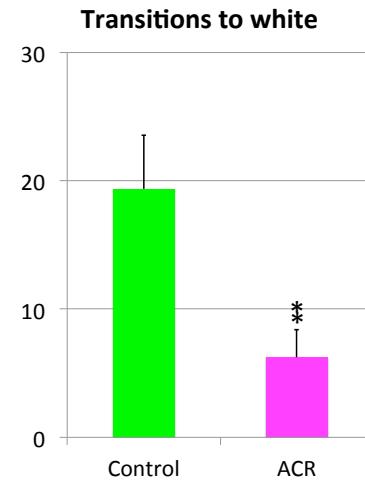
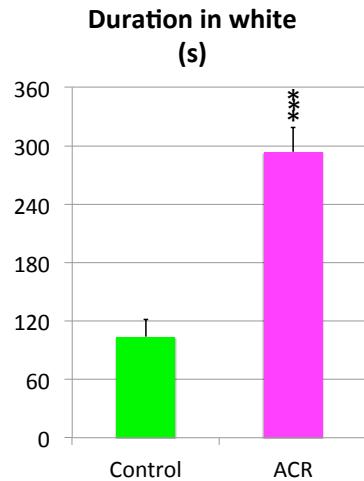
# Effects on behavior

## Dark-Light Test



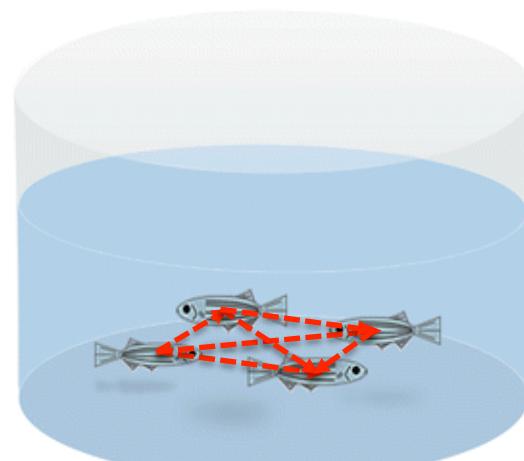
- ✓ Duration in white
- ✓ Transitions to white
- ✓ Average entry duration

# Negative scototaxis: increased time in white



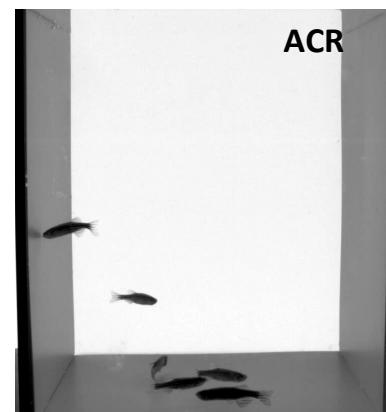
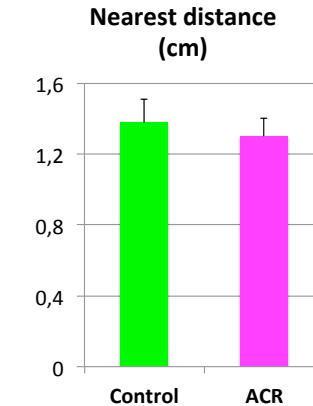
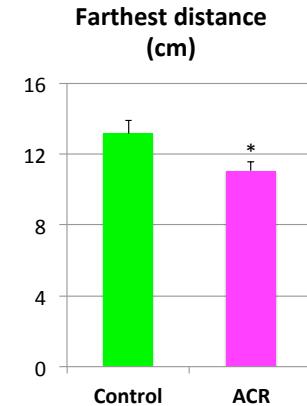
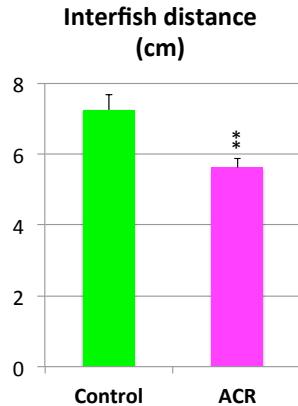
# Effects on behavior

## Social behavior: Shoaling

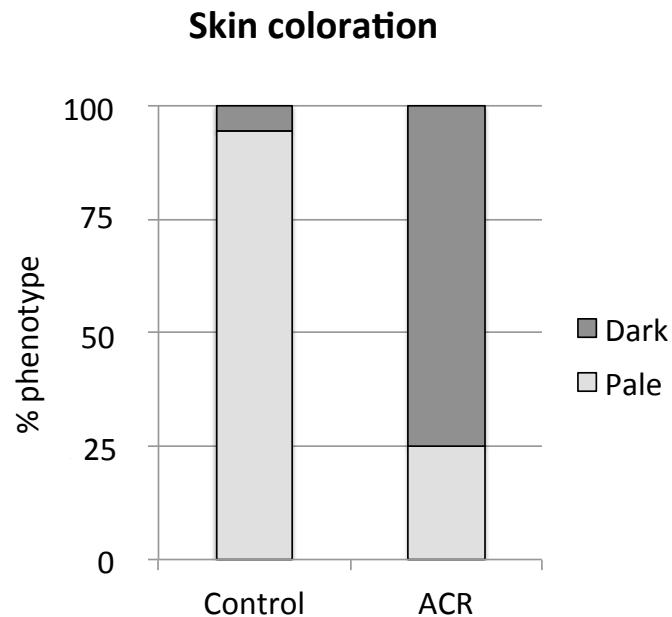
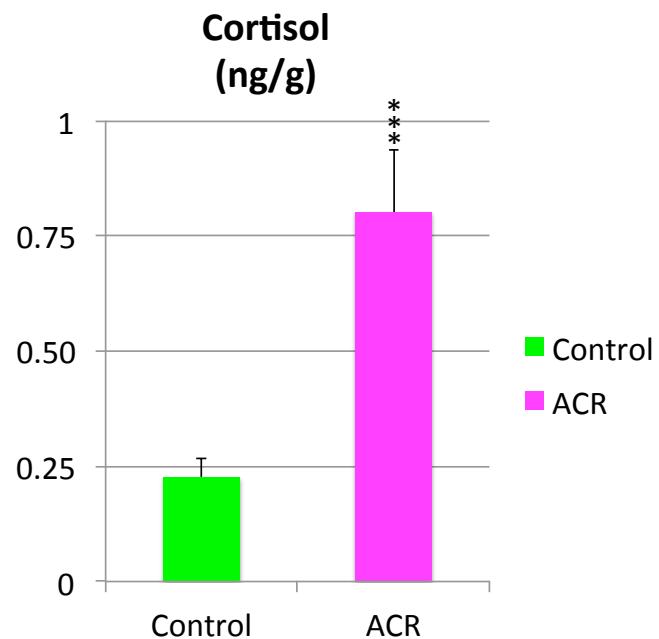


Lateral view

# Increased social cohesion



# Effects on behavior



# Summarizing behavioral effects...

✓ Increased geotaxis (bottom dwelling), freezing and erratic movements → NTT

✓ Increase observed in the shoal cohesion → Shoaling test

↑↑ Cortisol



✓ Negative thigmotaxis (OFT) and scototaxis (DLT) — → Anxiety-like  
✓ Circling behavior

✓ Hypolocomotion (NTT and OFT)

✓ Droopy tail

✓ Dark coloration

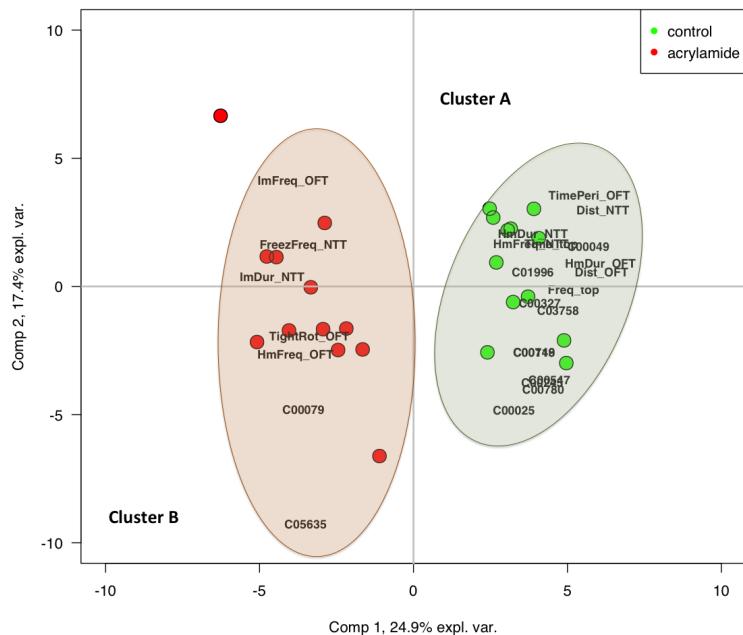
↑↑ Cortisol



Depression-like

# Effects on neurotransmitters

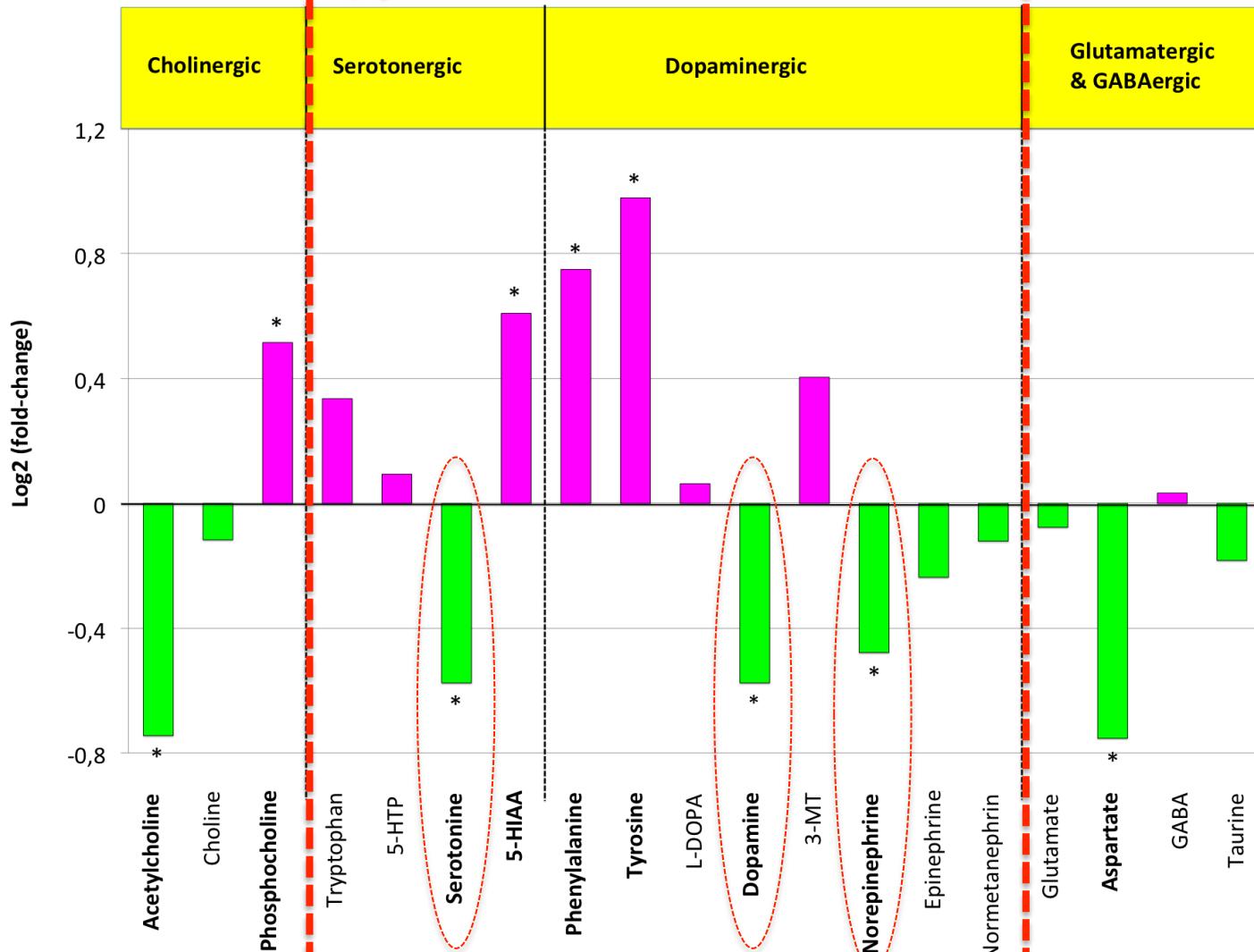
**a**



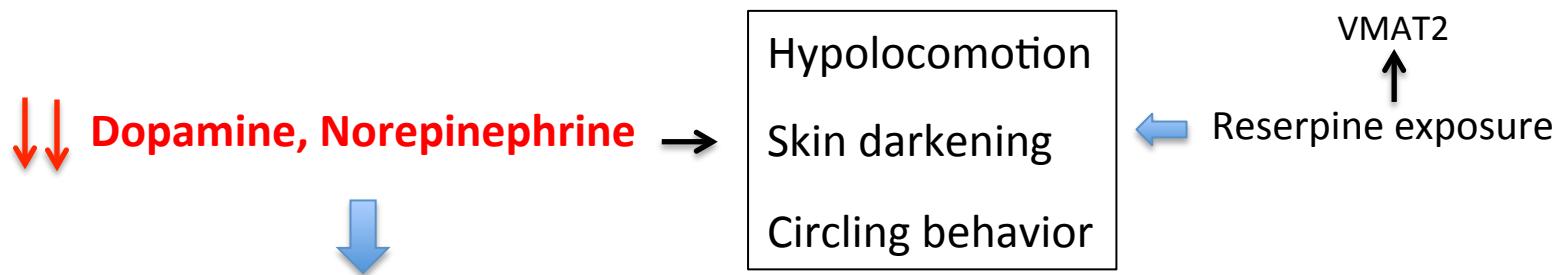
**b**

	Key	Parameter
Cluster A	C00025	Glutamate
	C00049	Aspartate
	C00148	Proline
	C00245	Taurine
	C00327	Citrulline
	C00547	Norepinephrine
	C00719	Betaine
	C00780	Serotonin
	C01996	Acetylcholine
	C03758	Dopamine
	Dist_NTT	Distance NTT
	Dist_OFT	Distance OFT
	Freq_top	Frequency in top
	HmDur_NTT	HM duration (NTT)
	HmDur_OFT	HM duration (OFT)
Cluster B	HmFreq_NTT	HM frequency (NTT)
	Time_top	Time in top (NTT)
	TimePeri_OFT	Time in periphery (OFT)
	C00079	Phenylalanine
	C05635	5-HIAA
	FreezFreq_NTT	Freezing frequency
	HmFreq_OFT	HM frequency (OFT)
	ImDur_NTT	Immobility duration (NTT)
	ImFreq_OFT	Immobility frequency (OFT)
	TightRot_OFT	Tight rotations

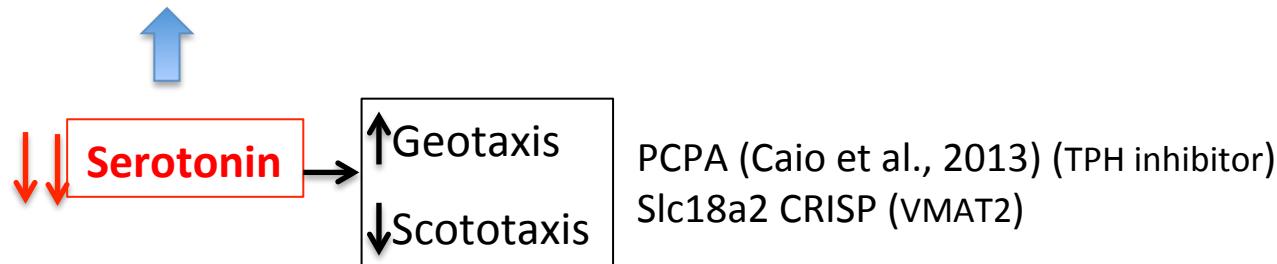
## ↓↓ Monoaminergic systems

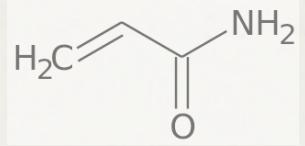


# Neurochemical and neurobehavioral changes in depression-like phenotypes



## Depression-like behavior in rodent and fish





**Acrylamide exposure induces a complex behavioral phenotype, characterized by depression comorbid with anxiety**

# Thank you for your attention!



Melissa Faria  
Cristian Gómez-Canela  
Eva Prats  
Juliette Bedrossiant  
Benjamin Piña  
Romà Tauler



SFP-984777



CTM2017-83242-R



Grant No. 2016 BP 0023



Leobardo Manuel Gómez-Oliván  
Karen Adriana Novoa-Luna



**TECHNION**  
Israel Institute of Technology

Arie Admon  
Tamar Ziv  
Shani Ben-Lulu



Grant No. 1775/12