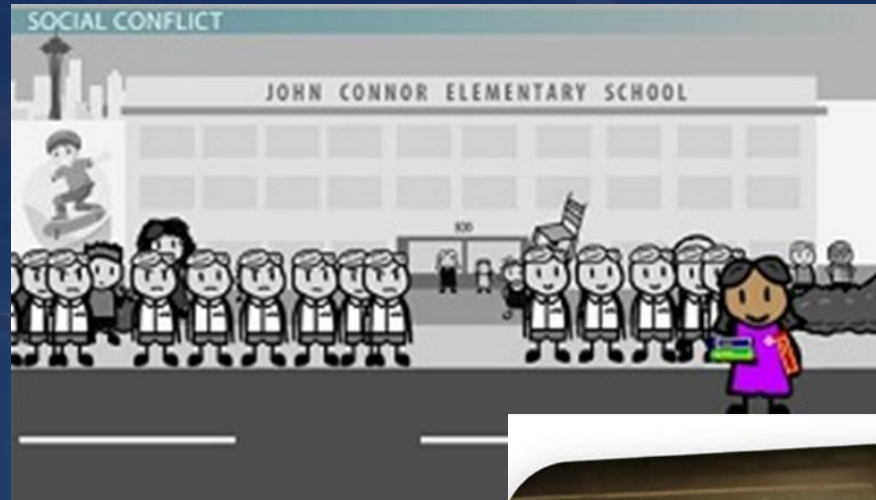
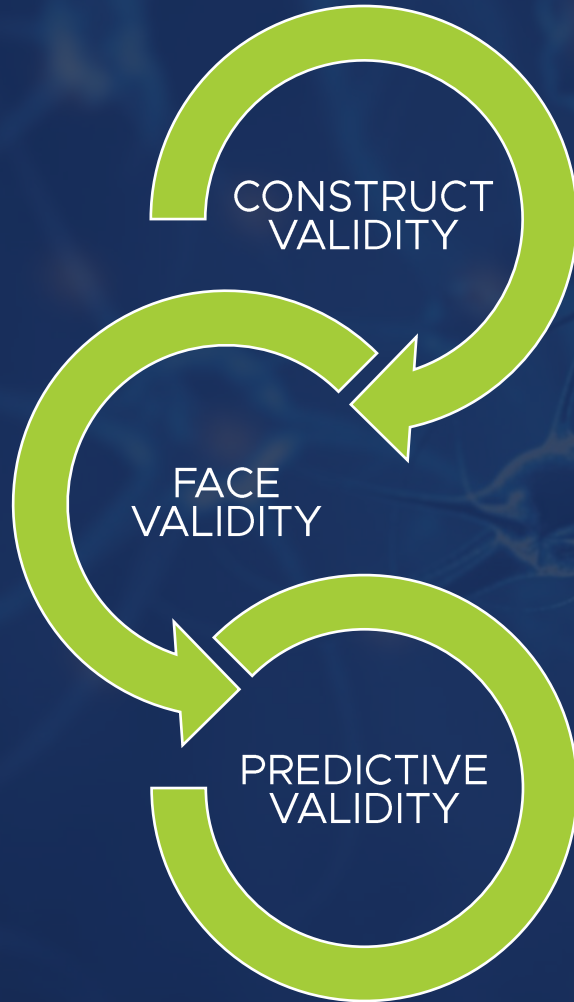


# Stress-based animal models - refinement vs. translation

Do we fully understand what we are doing?



Chronic, lifetime stress is a strong predictor for the development of depressive symptoms.

# Chronic Social Defeat (CSD): a psychosocial model of depression in mice

## STEP 1: CD-1 aggression screening

- Selection of aggressors
- Once a day for 3 consecutive days

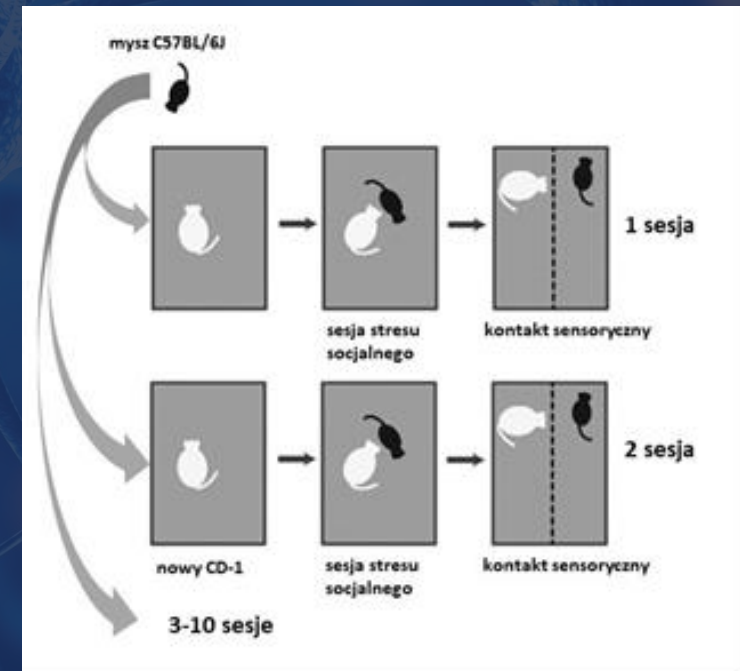


### Aggression criteria:

- CD-1 must attack in at least two consecutive sessions
- The latency to initial aggression must be less than 90 sec.

## STEP 2: Chronic social defeat model

- Once a day for 10 consecutive days or twice a day for 5 consecutive days



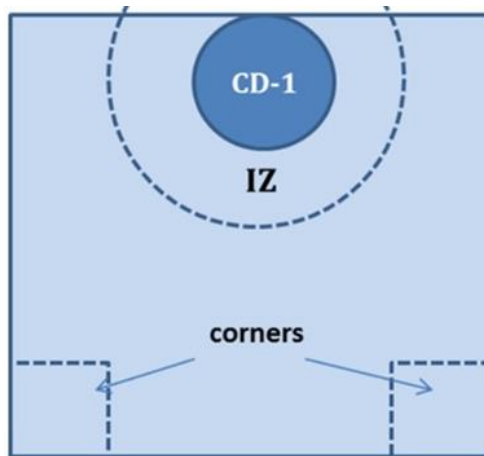
*Berton O. et al. 2006 Vol. 311 Science*

Animal ID:CSD1_6			27.10.202	28.10.2020	29.10.2020	30.10.2020	31.10.2020	01.11.2020	02.11.2020	03.11.2020	04.11.2020
			D1	D2	D3	D4	D5	D6	D7	D8	D9
Body weight (g)			22,6	22	22,6	22,9	22,8	22,8	22,8	22,7	22,9
Change in body weight (g)			N/A	-0,6	0,6	0,3	-0,1	0	0	-0,1	0,2
Change in body weight (%)			N/A	-2,65487	2,727273	1,327434	-0,43668122	0	0	-0,4386	0,881057
Performed by: Ewa Sokolowska, Erwina Stojek, Danka Kozareva											
Animal ID:		Date	27.10.202	28.10.2020	29.10.2020	30.10.2020	31.10.2020	01.11.2020	02.11.2020	03.11.2020	04.11.2020
Aggressor											
Parameter	Observation	Score	D1	D2	D3	D4	D5	D6	D7	D8	D9
Body weight*	Unchanged or <5% loss	0	N/A	0	0	0	0	0	0	0	0
	5-10% loss	1									
	>10% loss	2									
Physical appearance	Normal	0	0	0	0	0	0	0	0	0	0
	Lack of grooming	1									
	Ocular or nasal discharge	2									
	Hunched posture	4									
Respiratory signs	Normal breathing	0	0	0	0	0	0	0	0	0	0
	Slightly laboured breathing	1									
	Notably laboured breathing	3									
Behaviour	Normal	0	0	0	0	0	0	0	0	0	0
	Minor changes	1									
	Reduced mobility and/or alertness	2									
	Unprovoked vocalisations, hyperactivity or immobility	6									
Wound healing	Normal	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Discharge	1									
	Excessive discharge	2									
	Open wound	5									
Other observations											
<b>TOTAL</b>			<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
Score	Intervention required										
0-4	Continue to monitor as normal.										
5_9	Monitor regularly. Analgesia may be required.										
10_14	Analgesia required. Notify animal care and welfare officer (ACWO) and/or designated veterinarian (DV). Consider euthanasia.										
15-18	Euthanasia.										

# The Social Preference Test / Social Preference Distribution

CSD leads to the development of marked social aversion.

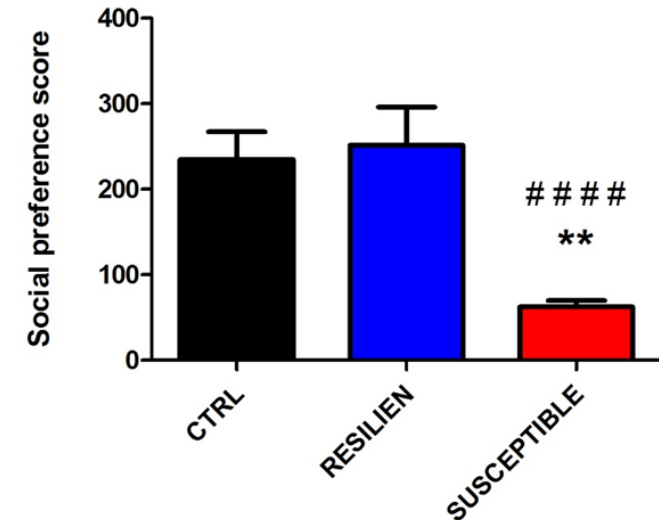
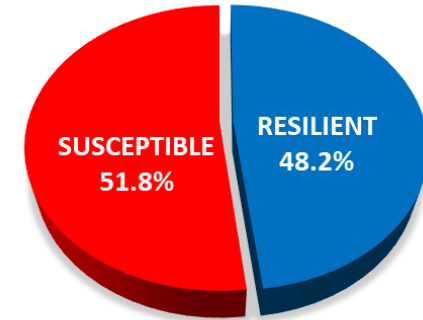
- 1<sup>st</sup> trial – “no target” (empty cylinder), 150 sec
- 2<sup>nd</sup> trial – “target” (“unfamiliar” CD1 in the cylinder), 150 sec



Time in Interaction Zone (IZ)  
with aggressor (2<sup>nd</sup> trial - “target”)

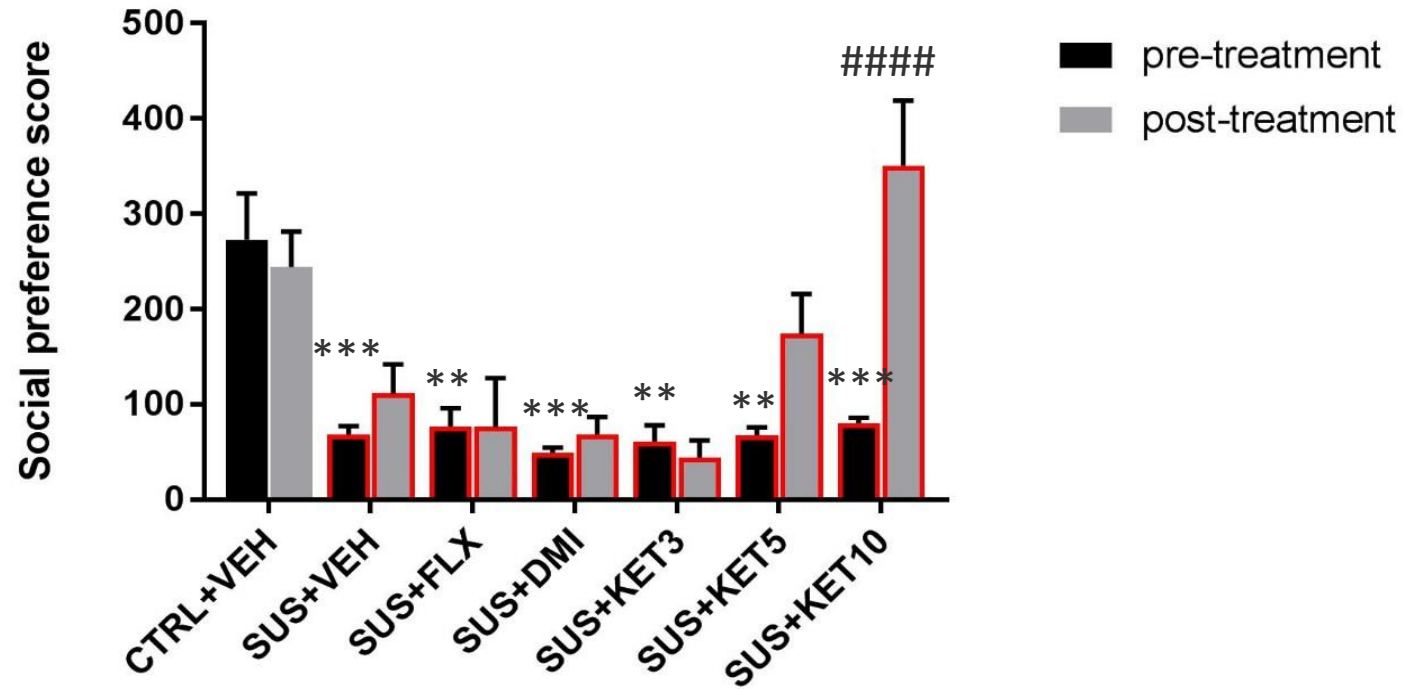
- **Social Preference (SP)** =  $\frac{\text{Time in Interaction Zone (IZ) with aggressor (2nd trial - "target")}}{\text{Time in Interaction Zone (IZ) without aggressor (1st trial - "no target")}}$

- **Resilient mice:** SP > 100%
- **Susceptible mice:** SP < 100%



n= 6-14 per group. Mean ± SEM, \*\*p < 0.005 vs. CTRL, ####p < 0.0001 vs. RESILIENT. One-Way ANOVA followed by Fisher's LSD test.

# Acute Antidepressant Effect on Social Avoidance Phenotype



Mean ± SEM, **FLX**: fluoxetine (10 mg/kg, s.c.), **DMI**: desipramine (10 mg/kg, s.c.), **KET3**: ketamine (3 mg/kg, s.c.), **KET5**: ketamine (5 mg/kg, s.c.), **KET10**: ketamine (10 mg/kg, s.c.); (n = 6-12).

\*\* $p < 0.005$ , \*\*\* $p < 0.001$  vs. **CTRL+VEH pre-treatment**, #### $p < 0.0001$  vs. **pre-treatment**. Two-way ANOVA followed by Fisher's LSD test.

# Thank you.

Please feel free to contact us at any time to discuss your requirements or future projects that you have in mind.



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