Deep phenotyping of social behavior in animal models of ASD

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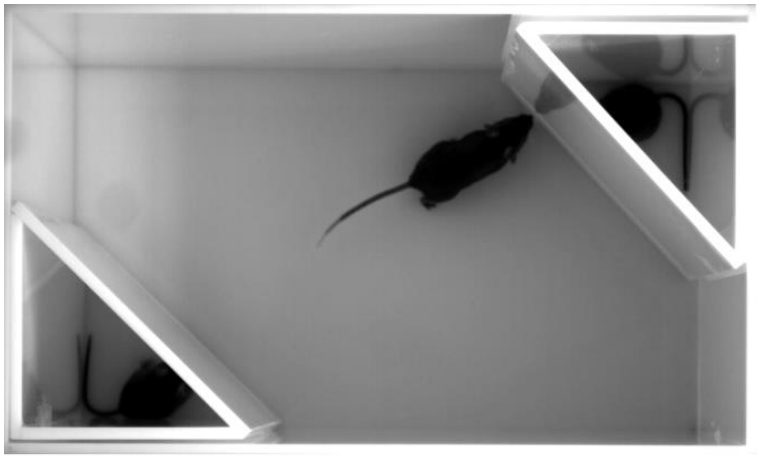
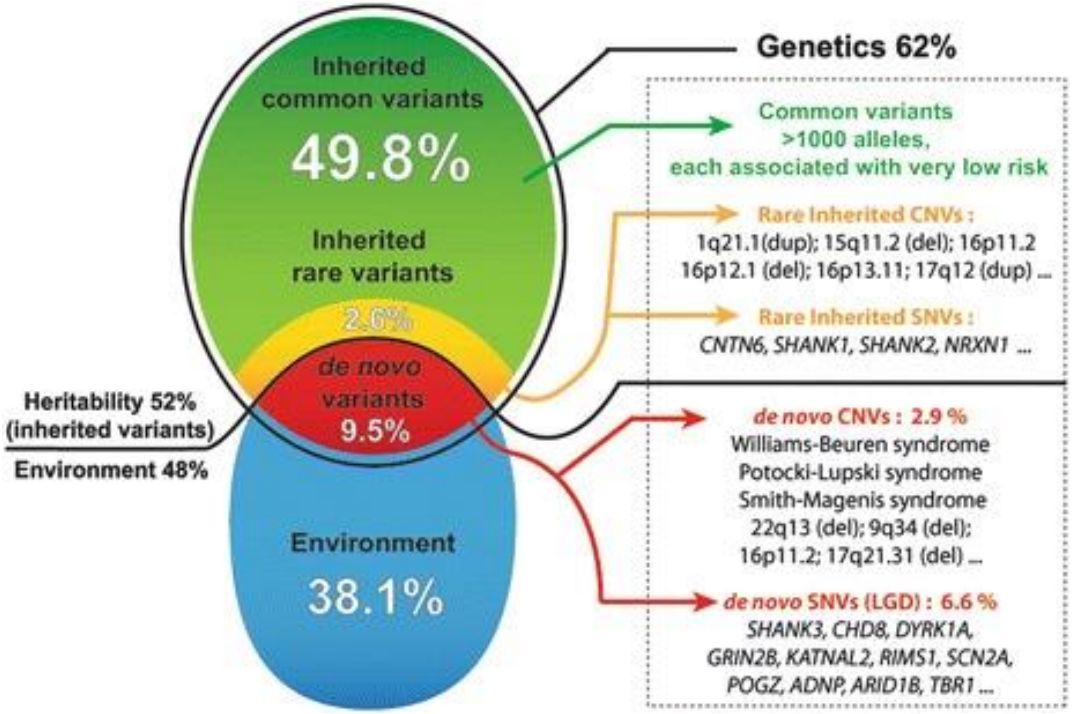


Israeli Meeting for Autism Research

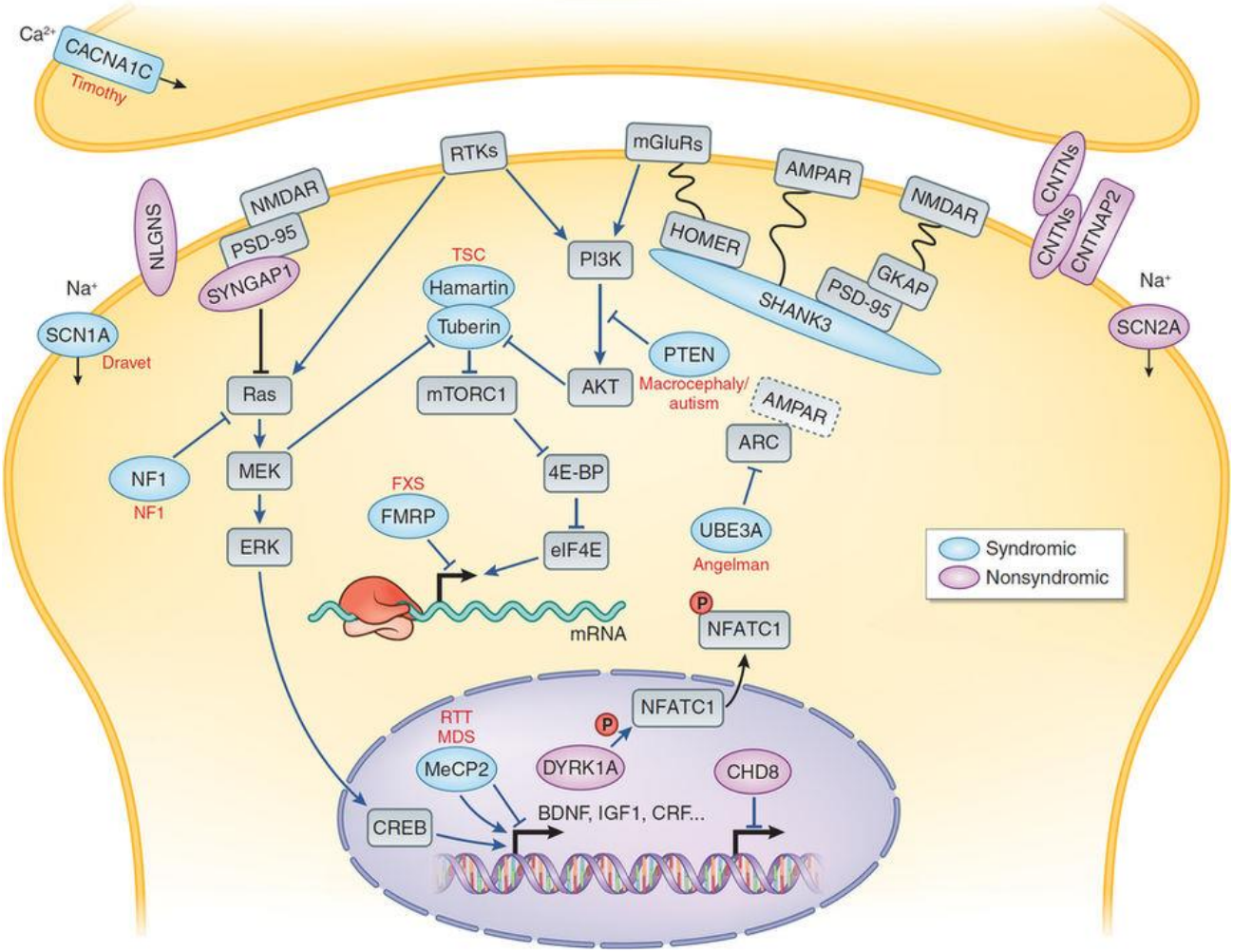
February 13th, 2019

Autism genetics



Adopted from: **The Genetics of Autism Spectrum Disorders**
Guillaume Huguet, Marion Benabou, and Thomas Bourgeron.
In: A Time for Metabolism and Hormones [Internet].
Sassone-Corsi P, Christen Y, editors. Cham (CH): Springer; 2016.

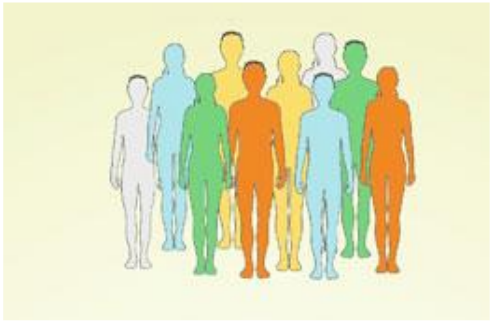
Syndromic ASD



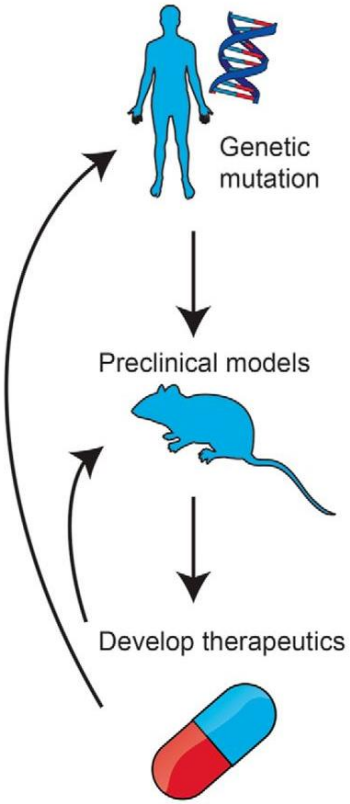
Adopted from: Lessons learned from studying syndromic autism spectrum disorders, Yehezkel Sztainberg & Huda Y. Zoghbi, *Nature Neuroscience* **19**, 1408–1417 (2016)

The problem with CNVs

Small cohorts, high heterogeneity



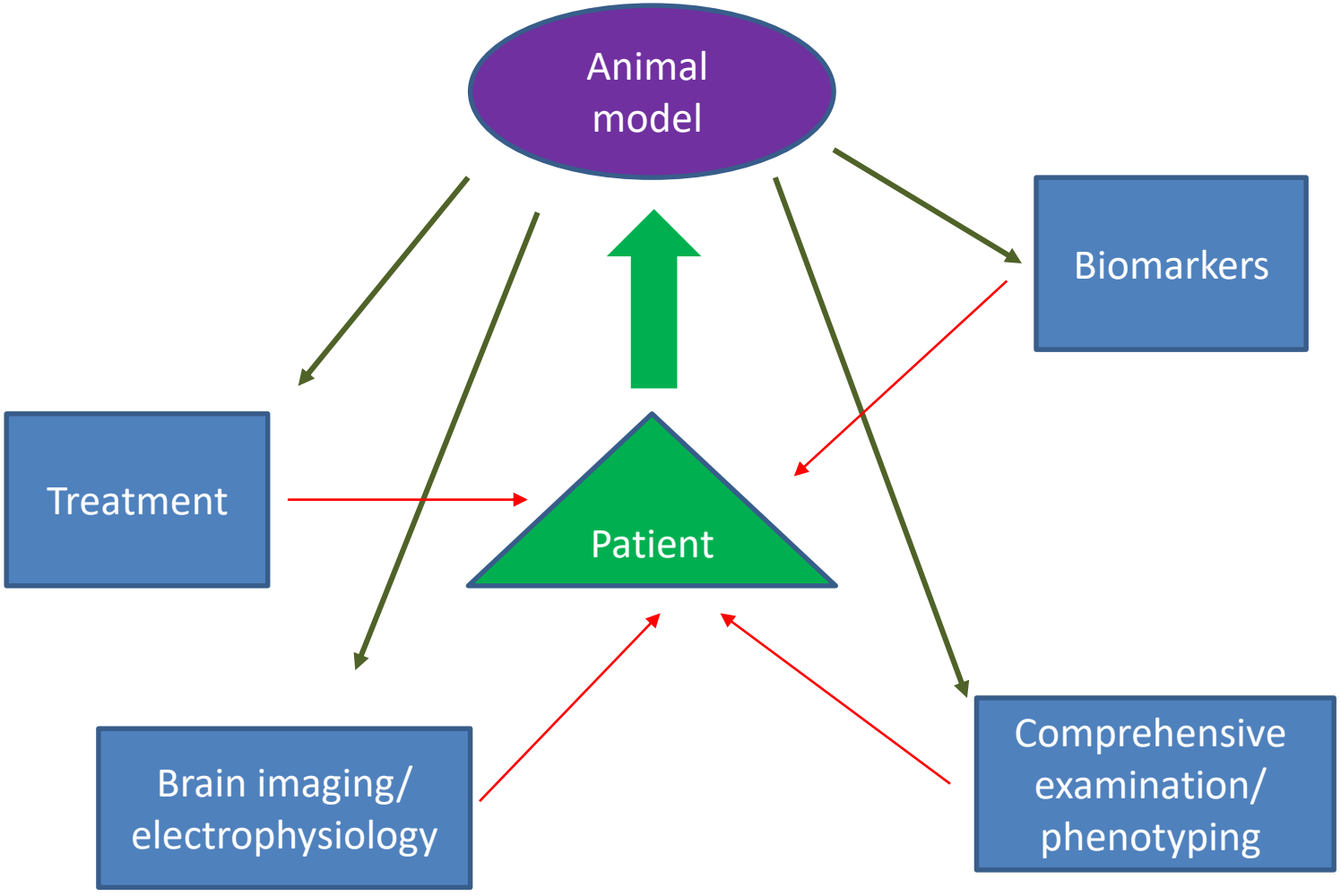
Personalized medicine



Animal models of rare CNVs

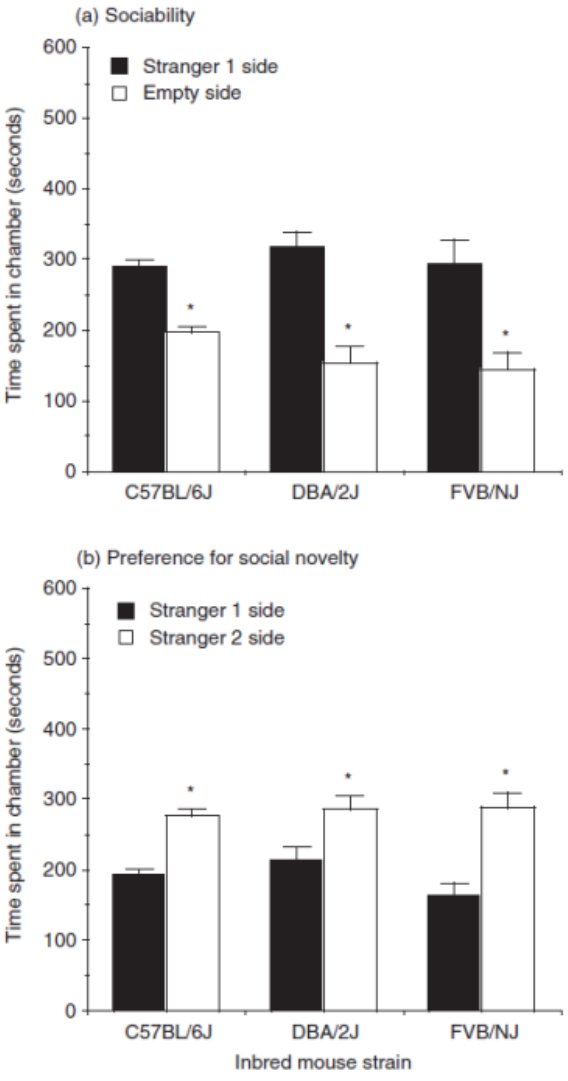
Homogeneous, large population of animals carrying the CNV or part of it

and they actually behave

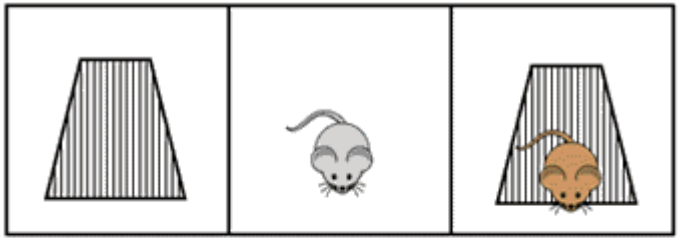

Animal model
Biomarkers
Treatment
Patient
Brain imaging/ electrophysiology
Comprehensive examination/ phenotyping

Behavioral phenotyping of social behavior in animal models

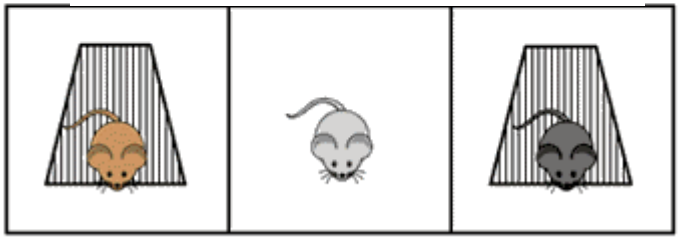
The three-chamber test



Adapted from Moy *et al*. Genes, Brain and Behavior (2004) 3: 287–302

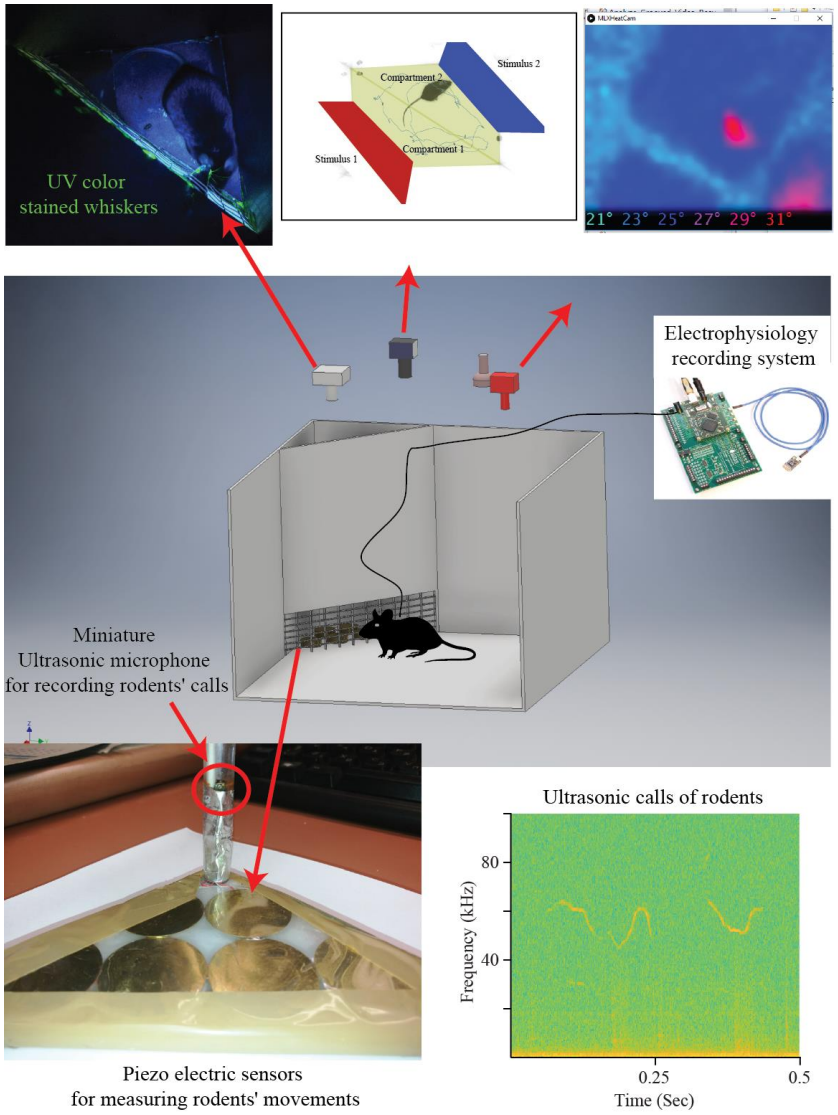


Social preference (sociability)

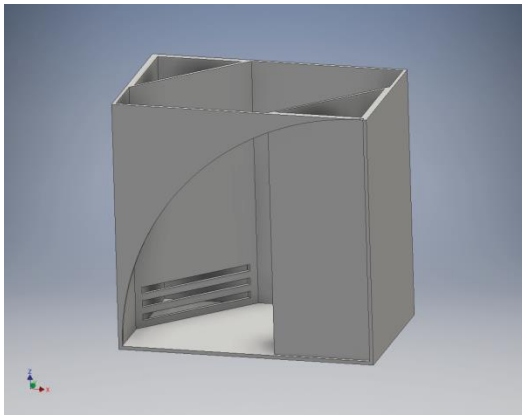


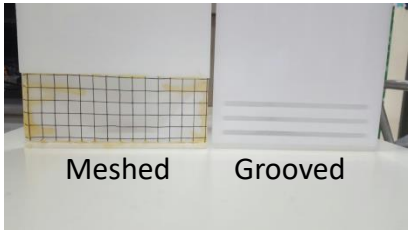
Social novelty preference

Towards deep phenotyping of social behavior in animal models



TrackRodent: A novel system for tracking social behavioral dynamics



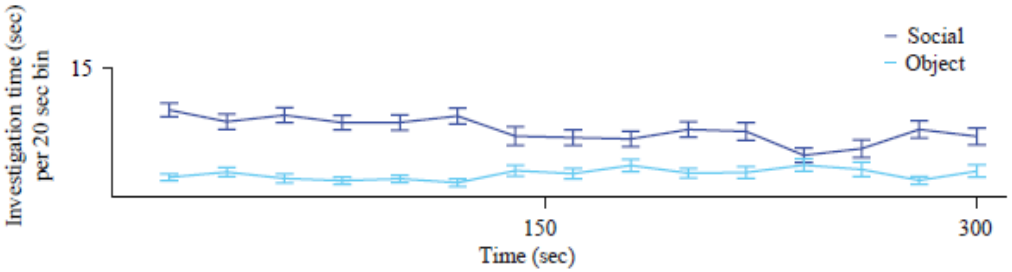


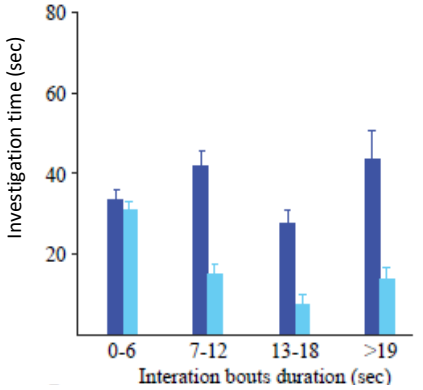
Eng. Alex Bizer

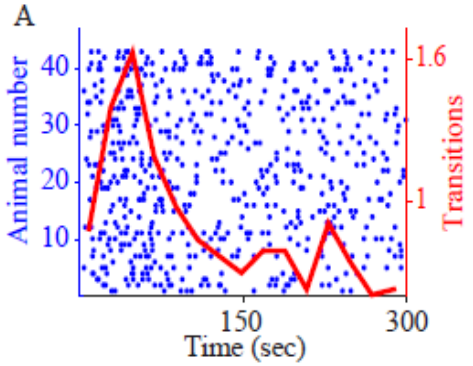
Dr. Shai Netser

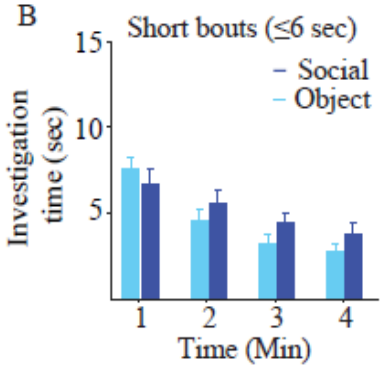
Netser *et al*. Molecular Autism 2017

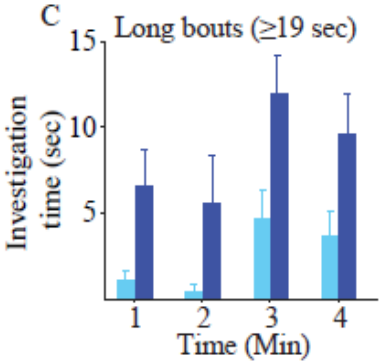
Social preference dynamics in C57BL/6J mice

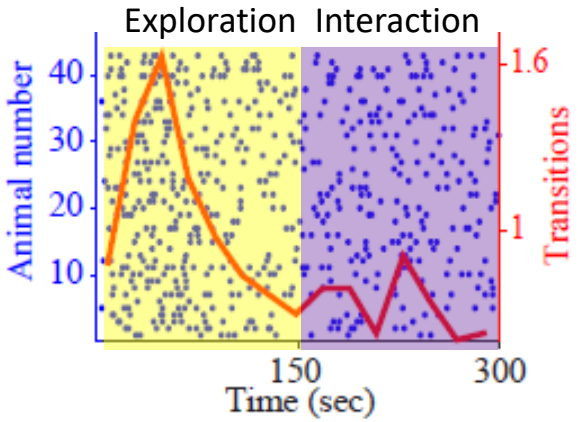




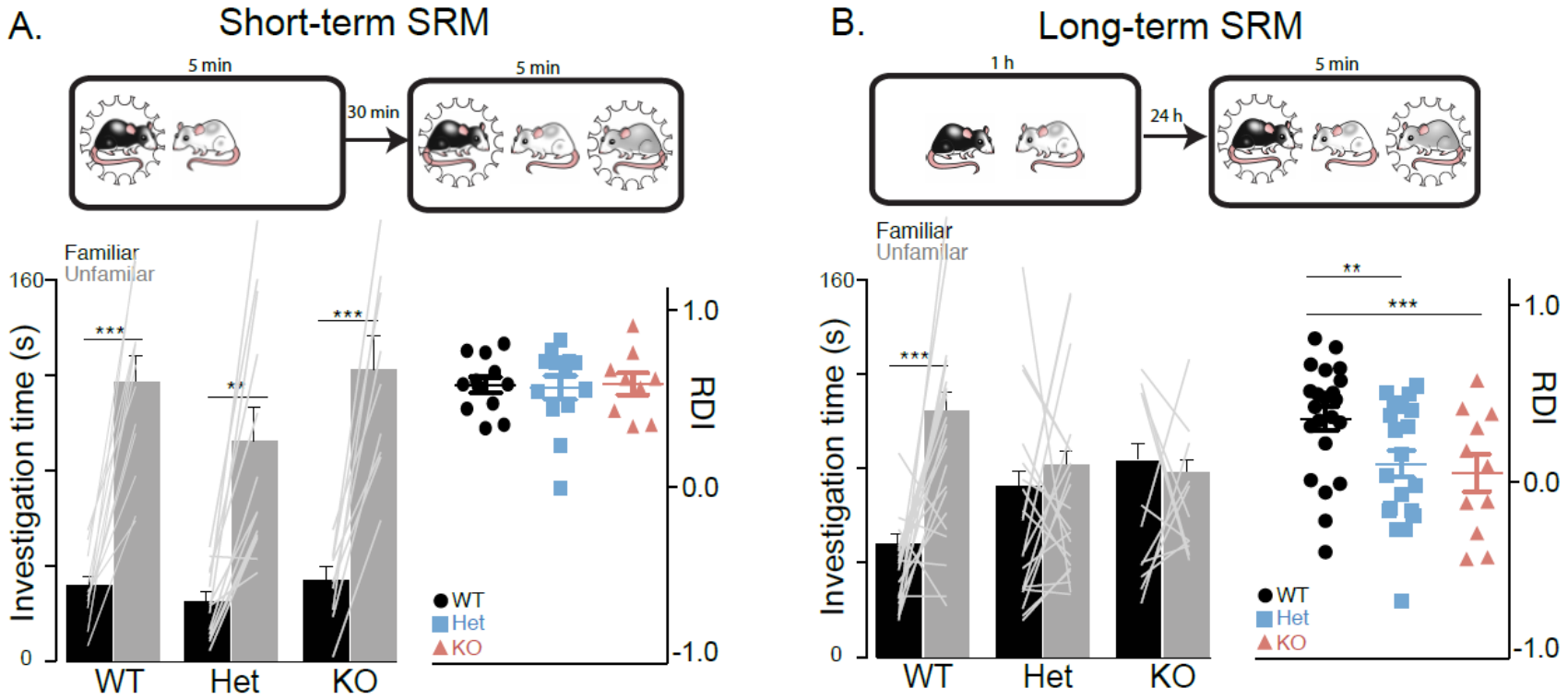








Shank3-deficient rats display a specific loss of long-term social recognition memory (SRM)



Harony-Nicolas *et al.*, 2017, ***eLife***

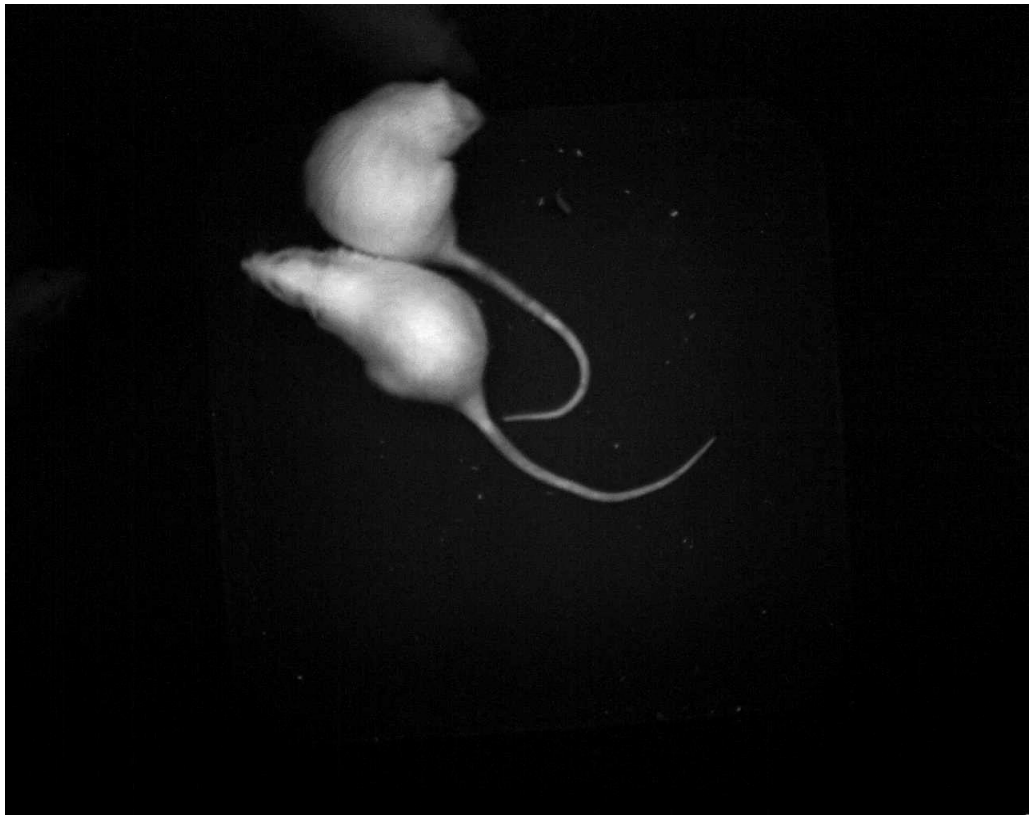
Experimental design

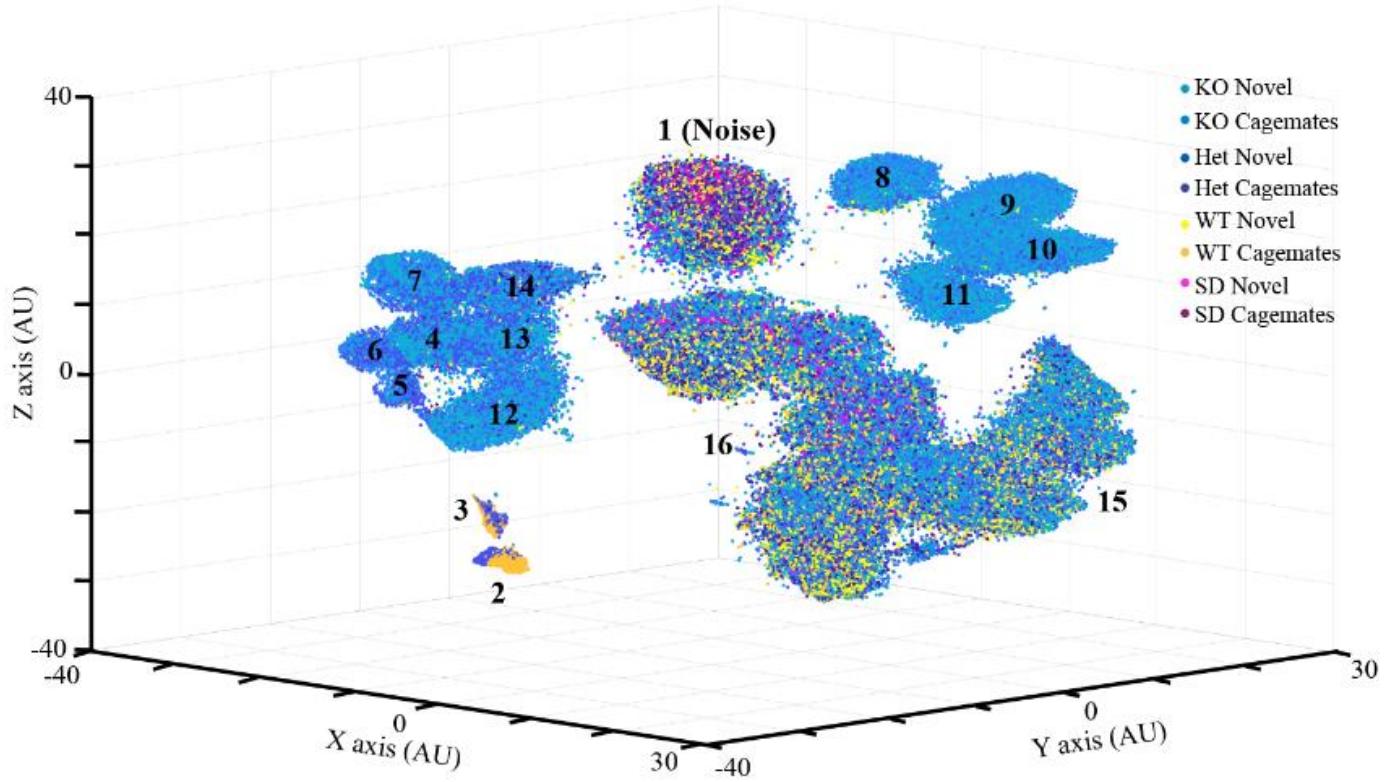
Dyadic interactions of animals, each pair of a distinct genotype, all males

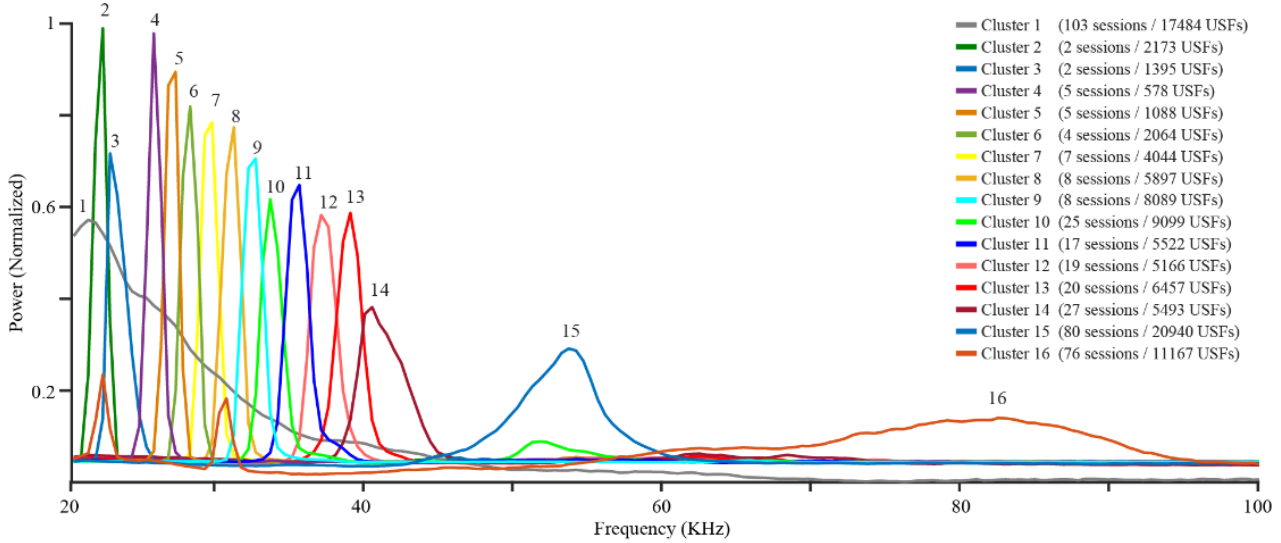
Each genotype was tested with either familiar or unfamiliar partners

4 genotypes (fam/unfam)

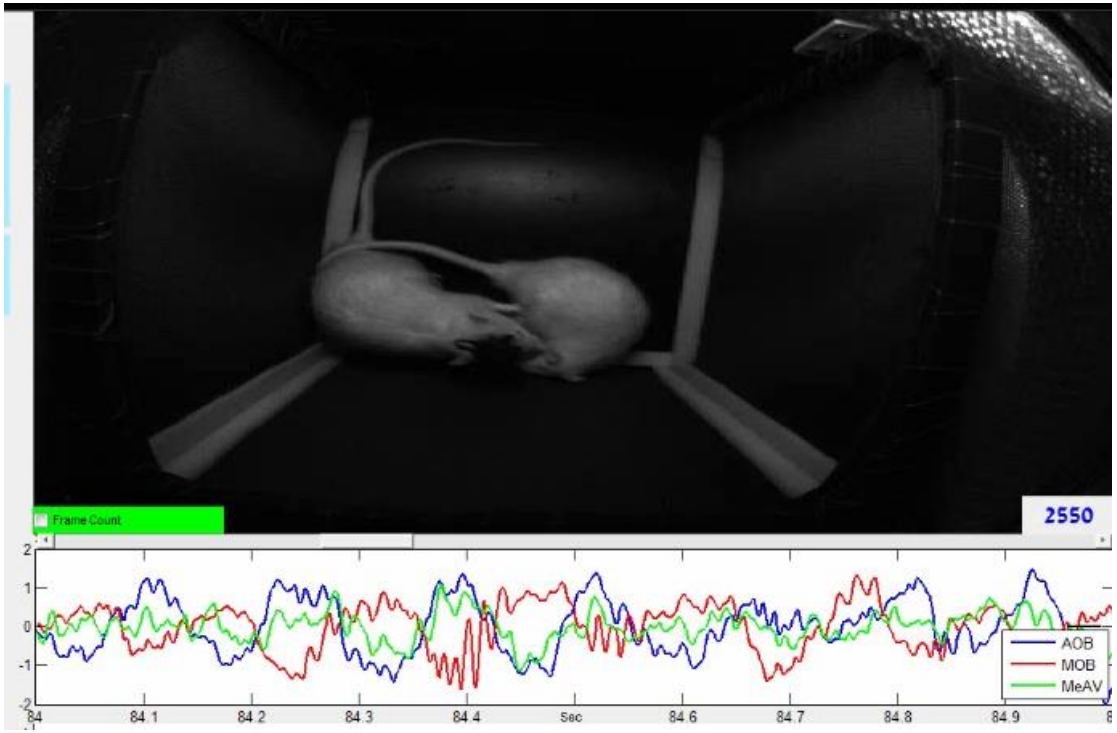
- SD rats (10/10)
- *Shank3*$^{+/+}$ (8/14)
- *Shank3* $^{+/-}$ (22/22)
- *Shank3* $^{-/-}$ (10/13)

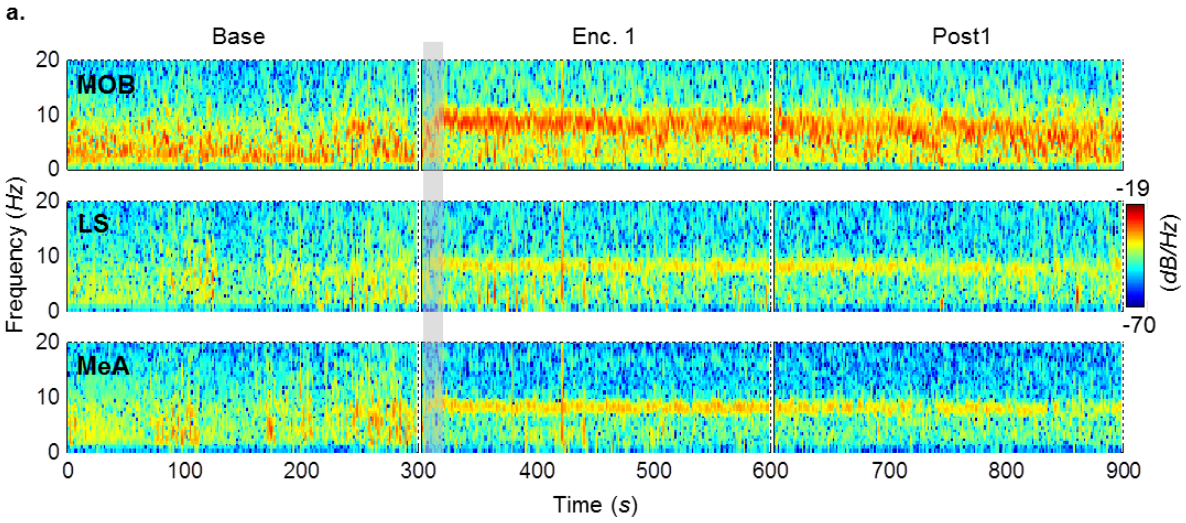



1 (Noise)
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
KO Novel
KO Cagemates
Het Novel
Het Cagemates
WT Novel
WT Cagemates
SD Novel
SD Cagemates
Z axis (AU)
X axis (AU)
Y axis (AU)
40
0
-40
30

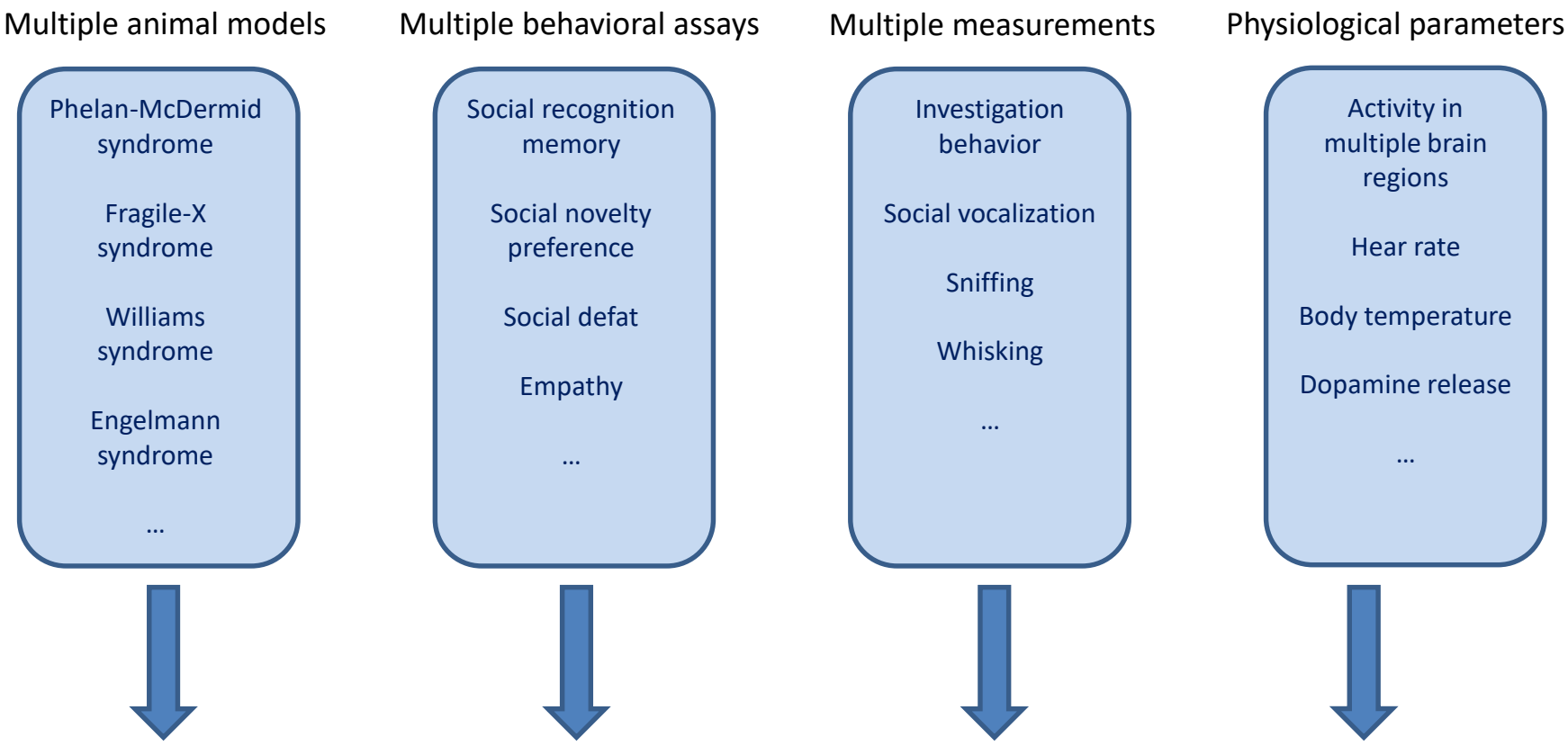

Power (Normalized)
Frequency (KHz)
1
0.6
0.2
20
40
60
80
100
Cluster 1 (103 sessions / 17484 USFs)
Cluster 2 (2 sessions / 2173 USFs)
Cluster 3 (2 sessions / 1395 USFs)
Cluster 4 (5 sessions / 578 USFs)
Cluster 5 (5 sessions / 1088 USFs)
Cluster 6 (4 sessions / 2064 USFs)
Cluster 7 (7 sessions / 4044 USFs)
Cluster 8 (8 sessions / 5897 USFs)
Cluster 9 (8 sessions / 8089 USFs)
Cluster 10 (25 sessions / 9099 USFs)
Cluster 11 (17 sessions / 5522 USFs)
Cluster 12 (19 sessions / 5166 USFs)
Cluster 13 (20 sessions / 6457 USFs)
Cluster 14 (27 sessions / 5493 USFs)
Cluster 15 (80 sessions / 20940 USFs)
Cluster 16 (76 sessions / 11167 USFs)

Theta rhythmicity as a correlate of social arousal





Vision



- Detailed analysis of deficits in social behavior, including its dynamics, correlated with changes in the emotional state of the animals and neural activity in the social brain.
- Detection and characterization of impaired mechanisms at the system level.
- Examination, in collaboration with other laboratories and companies, of various interventions which target the suspected mechanisms and aim to alleviate observed deficits