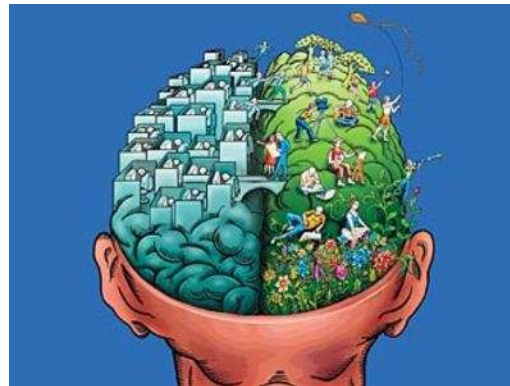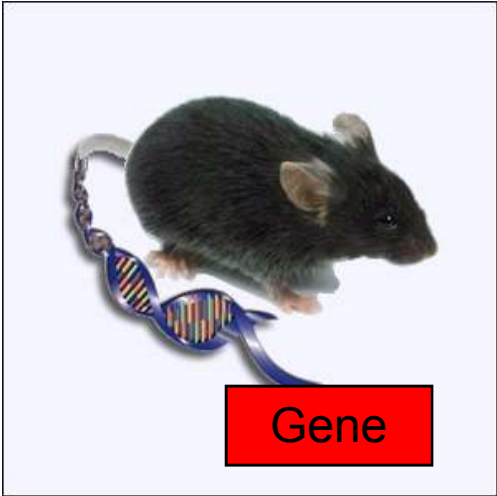# FROM INDIVIDUAL ENDOPHENOTYPES TO DYNAMIC INTERPLAY BETWEEN NEUROPSYCHIATRIC DOMAINS

Allan V Kalueff, PhD

ORNL, March 26, 2009

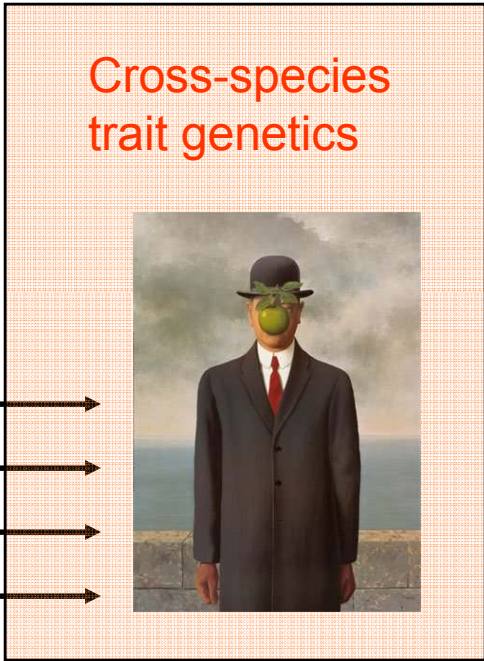Current neurophenotyping strategies

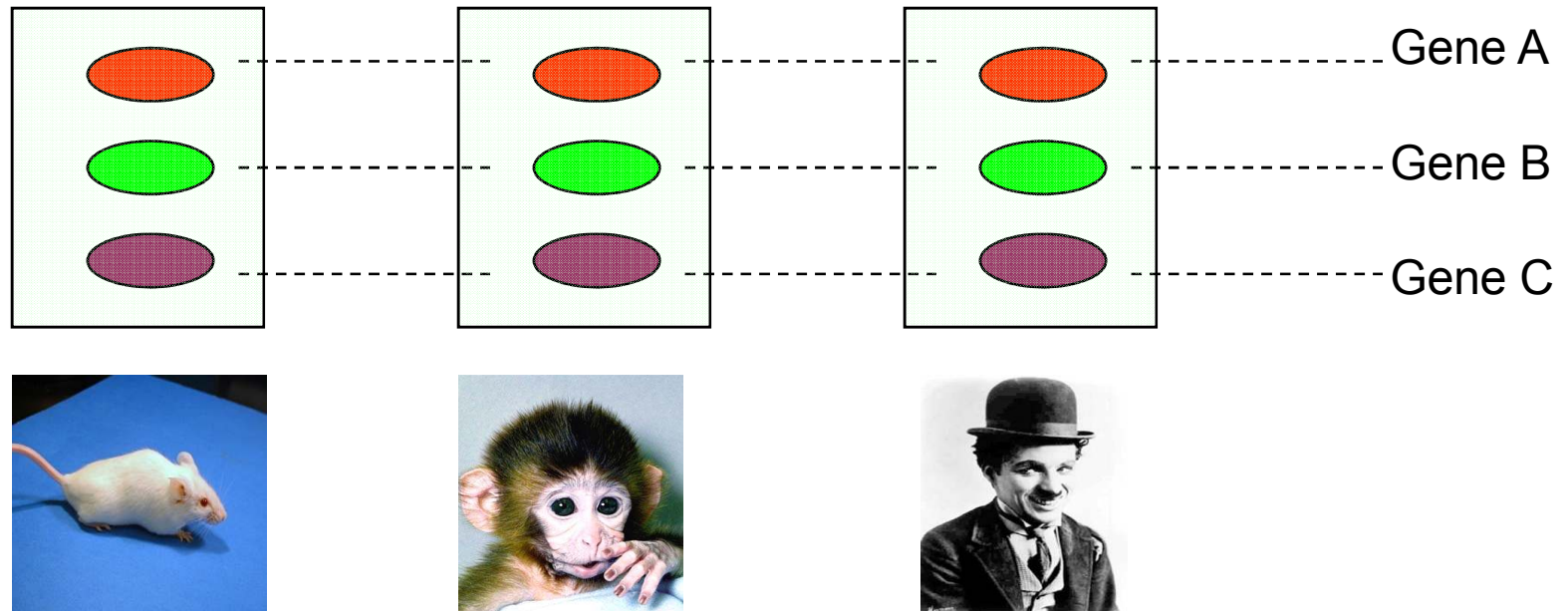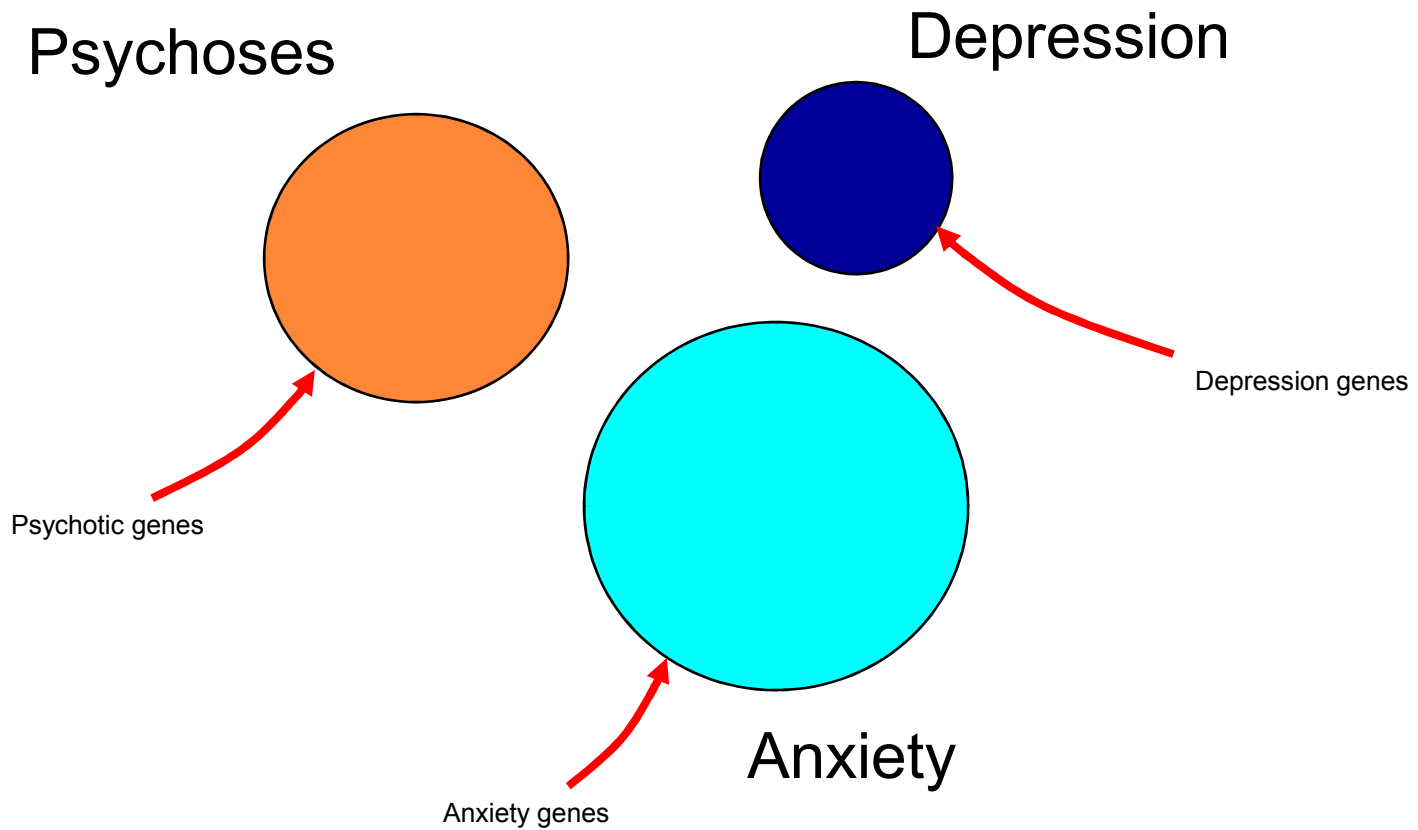# Cross-species trait genetics

Gene A

Gene B

Gene C

Pitfalls:
Not all behaviors are analogous in mice and men
Not all human endophenotypes are properly understood
Not all genes are homologous in mice and men
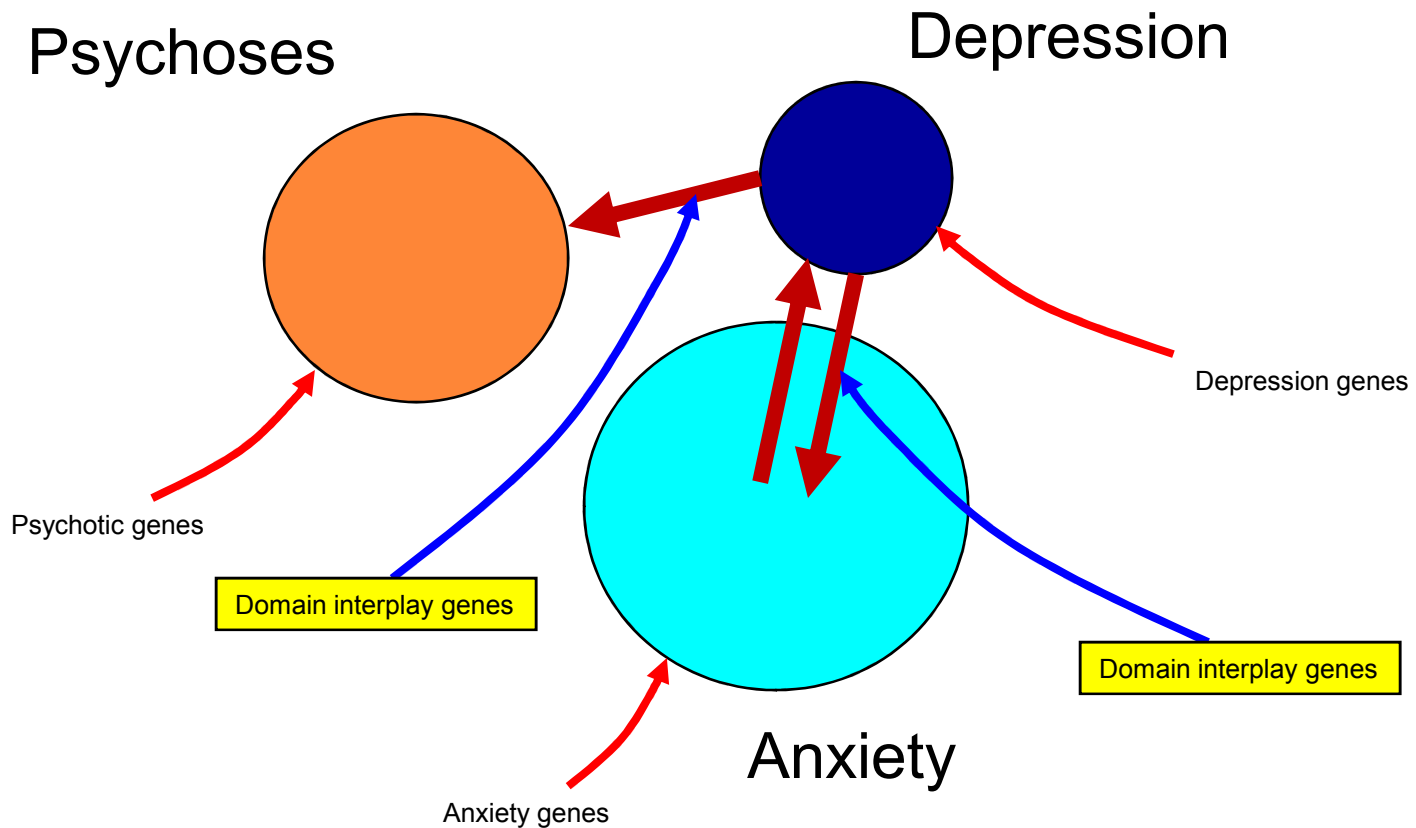Disorder-related phenomena frequently overlap

"Ideal" psychiatry

Psychoses

Depression

Anxiety

Psychotic genes

Depression genes

Anxiety genes

"Real" psychiatry: psychiatric spectra
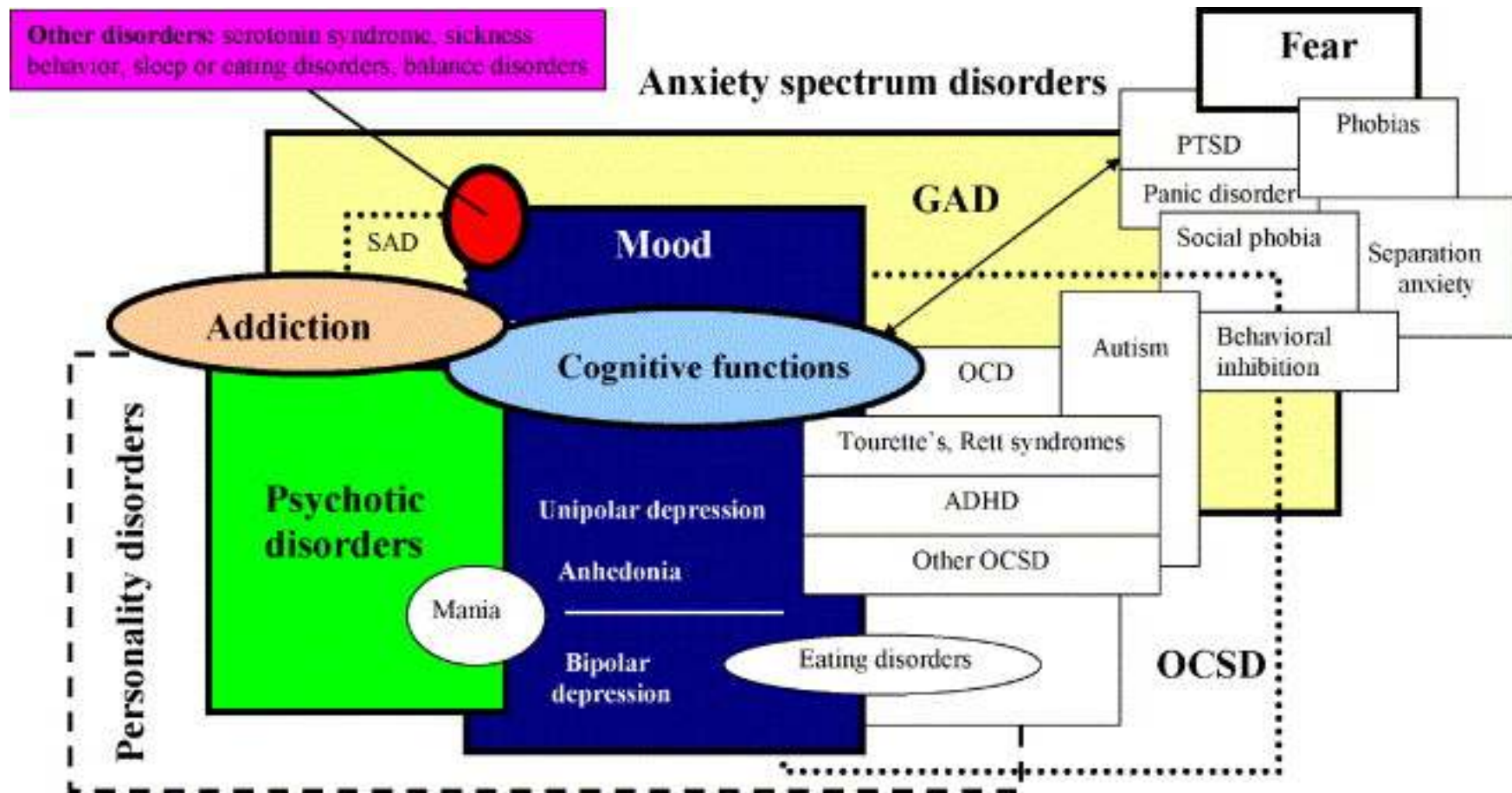
Kalueff et al., 2008

From domain genetics to domain interplay genetics

Kalueff et al., 2008, Behav Brain Res; Laporte et al., 2009, Behav Pharmacol
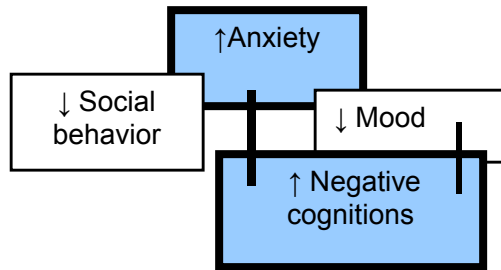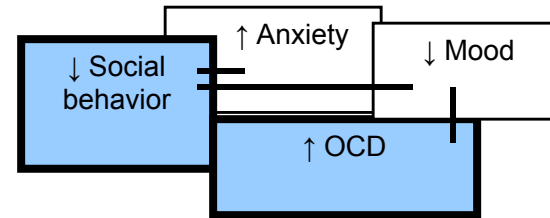
Domain interplay concept

Kalueff et al., 2008, Behav Brain Res
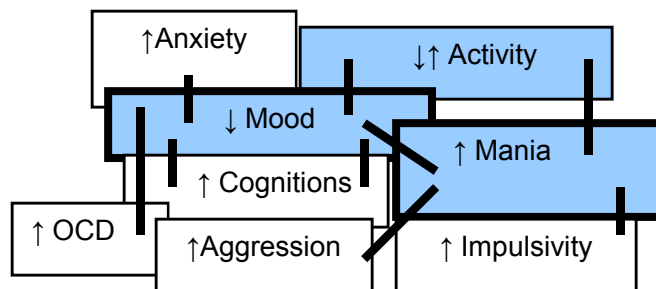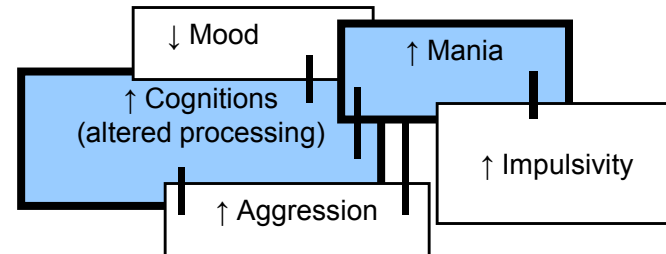Laporte et al., 2009, Behav Pharmacol

Post-traumatic stress disorder

↑Anxiety
↓ Social behavior
↓ Mood
↑ Negative cognitions

Autism

↑ Anxiety
↓ Social behavior
↓ Mood
↑ OCD

Bipolar depression

↑Anxiety
↓↑ Activity
↓ Mood
↑ Mania
↑ Cognitions
↑ OCD
↑Aggression
↑ Impulsivity

Schizophrenia

↓ Mood
↑ Mania
↑ Cognitions (altered processing)
↑ Impulsivity
↑ Aggression
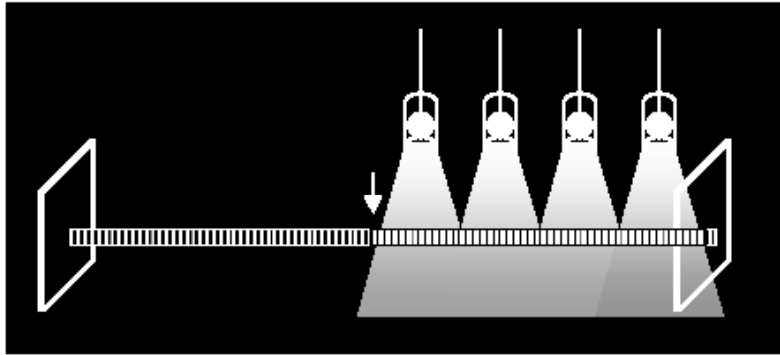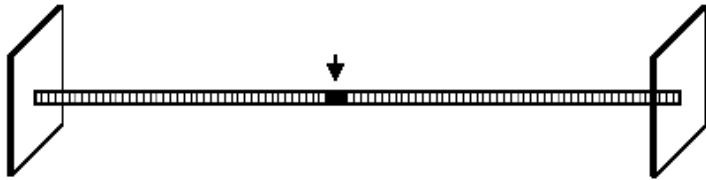
We need new approaches to modeling neuropsychiatric disorders

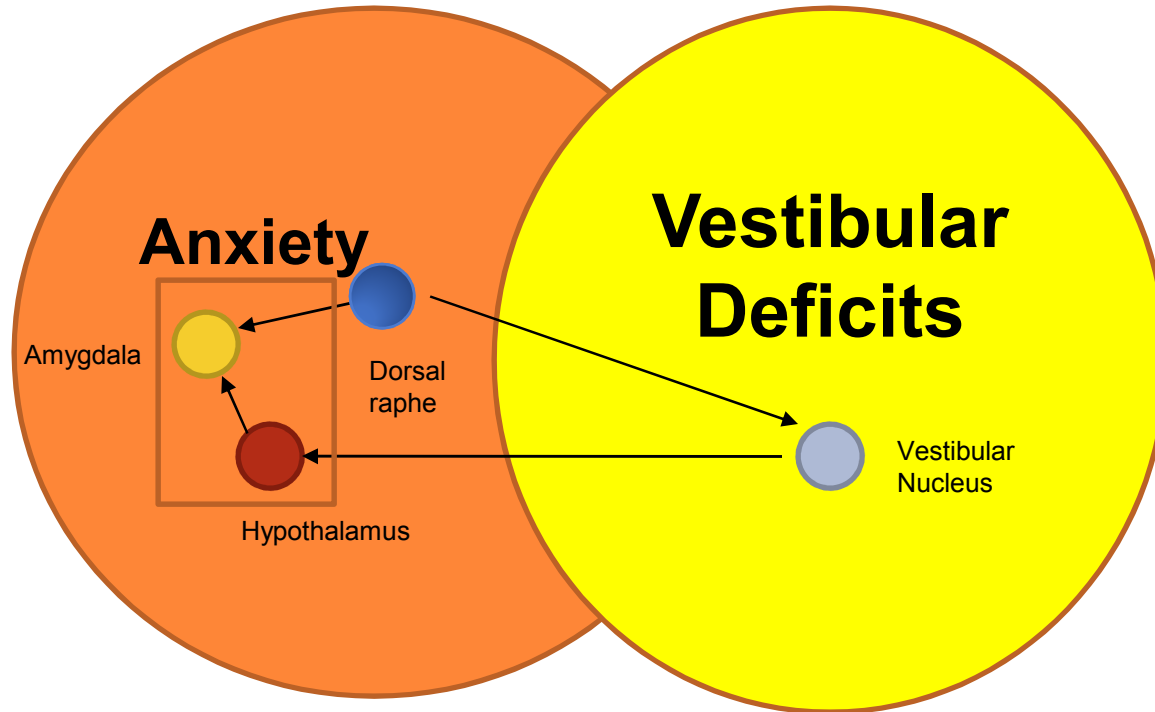# Creating new models of newly appreciated brain phenotypes
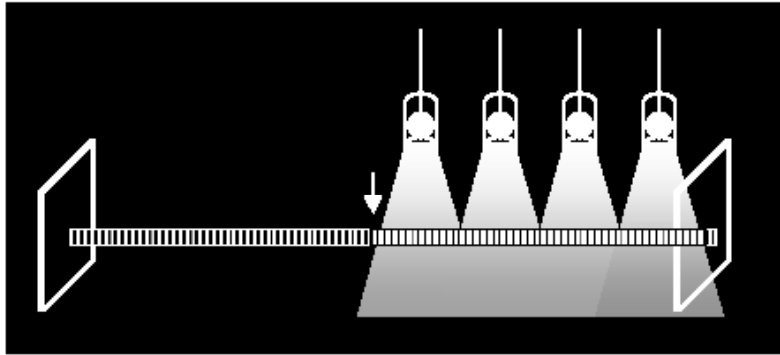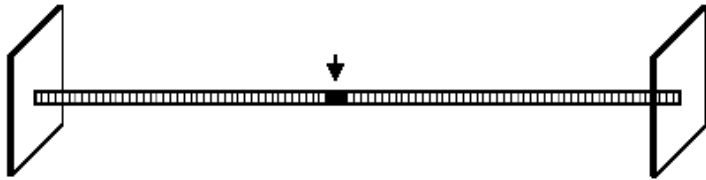

The rodent Suok ("ropewalking") test

Kalueff et al., 2005

OVERLAPPING BRAIN PATHWAYS

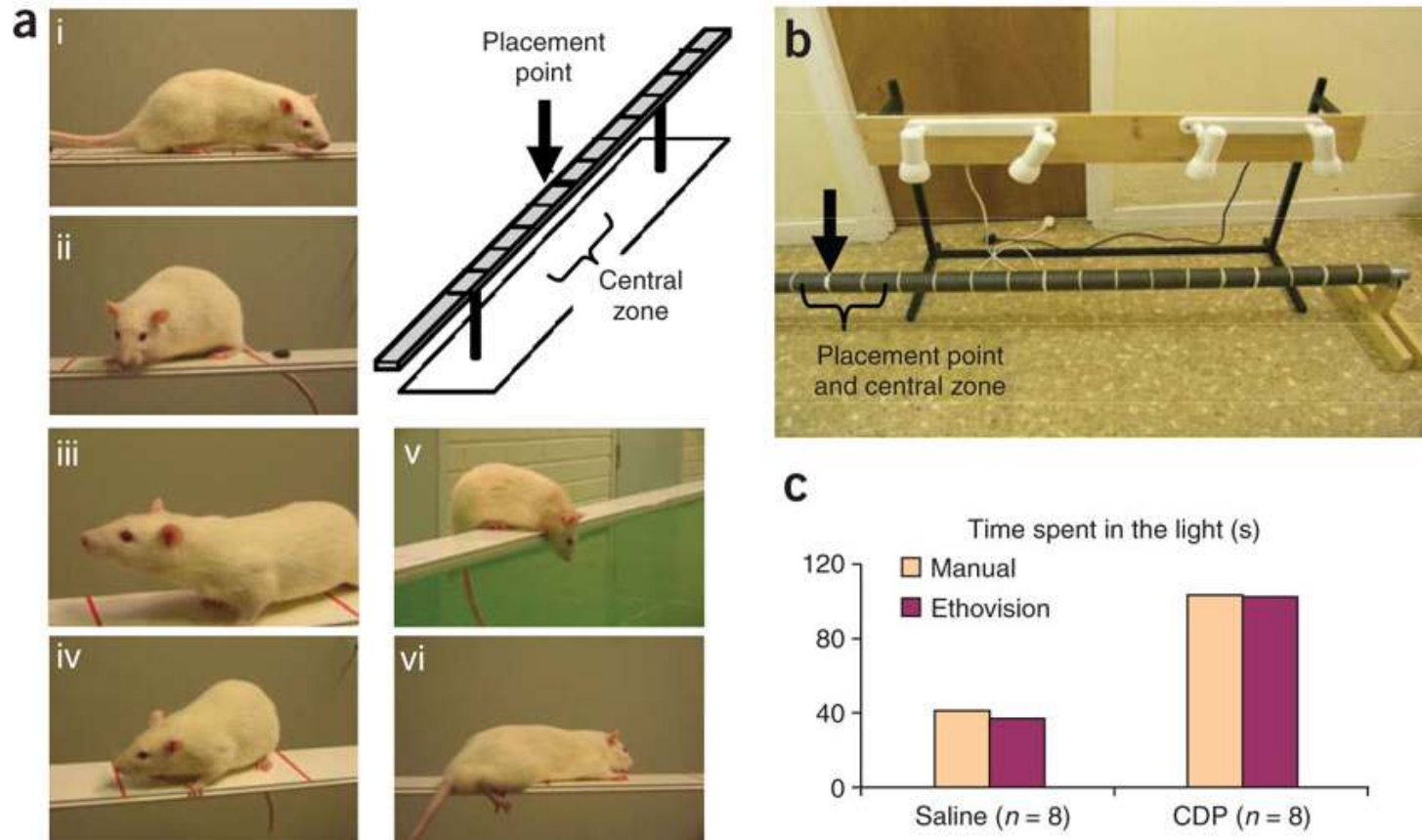# Creating new models of newly appreciated brain phenotypes
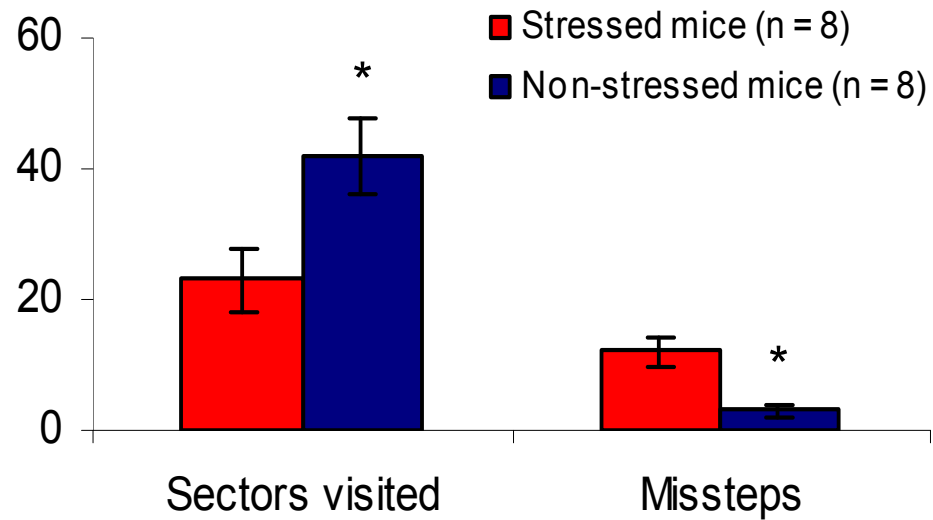

The rodent Suok ("ropewalking") test

Kalueff et al., 2005

The Rat Suok test of anxiety and balancing

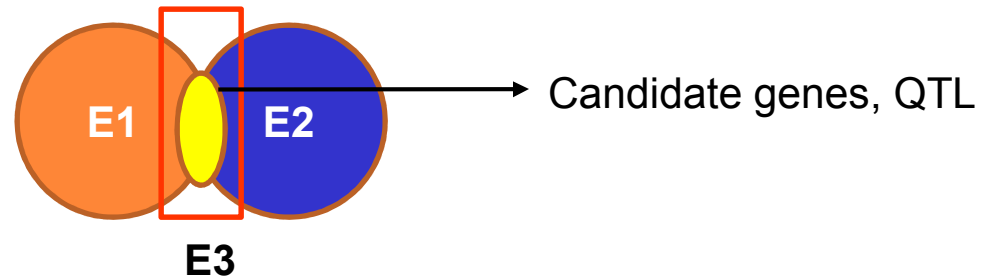
Kalueff et al., 2005

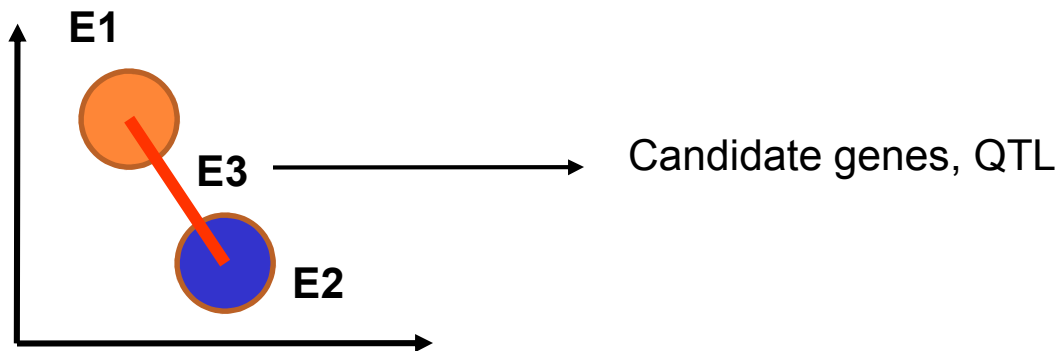# STRESS-EVOKED MOTORISENSORY DESINTEGRATION

We need new endpoints

Model newly appreciated brain phenomena/endophenotypes (e.g., SEMD)
   -> understand their genetics (candidate genes, QTL)

Candidate genes, QTL

Create new in-silico endophenotypes of "higher order"
                    -> understand their genetics (candidate genes, QTL)

Candidate genes, QTL

We need new endpoints

Model a transition from one disorder top another (e.g., anxiety-depression)
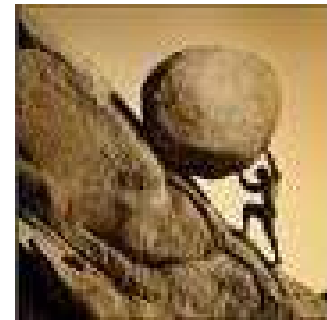-> understand their genetics (candidate genes, QTL)

Kudryavtseva et al., 2001

D1 —> D2

Candidate genes   Candidate genes

Unique candidate genes
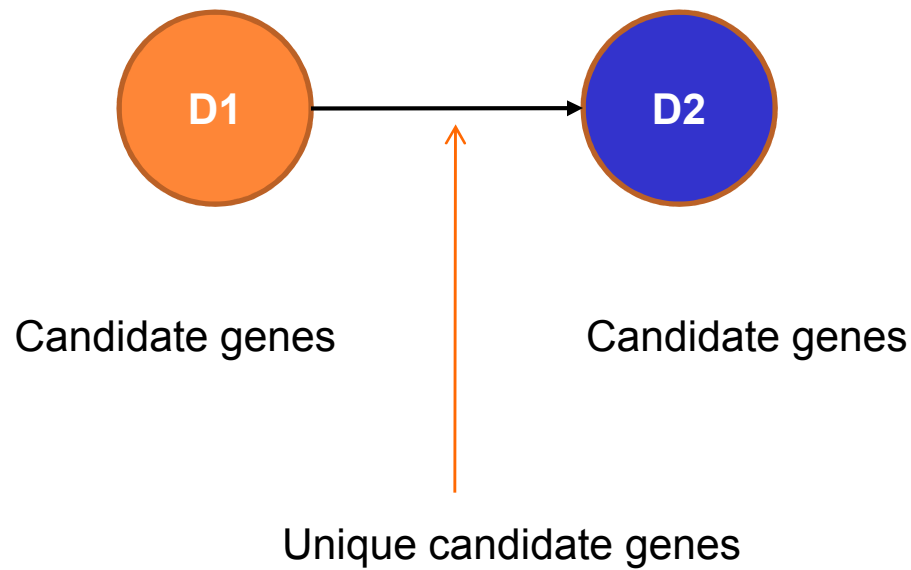
Other interacting domains of interest for our lab

- Stress [anxiety, depression] and obesity
- PTSD and OCD
- Stress and cancer
- Stress and autism

COLLABORATION IS WELCOME!

WWW.KALUEFFLAB.COM