

STANDARDIZING, HETEROGENIZING, OR DOMAIN INTERPLAY-BASED MODELLING?

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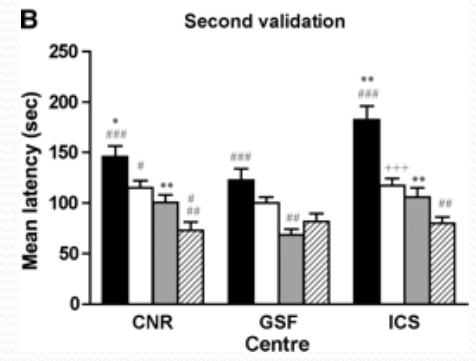
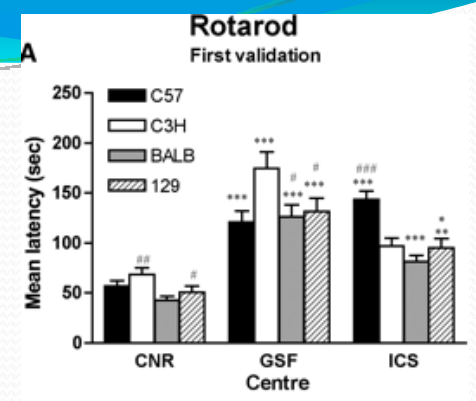
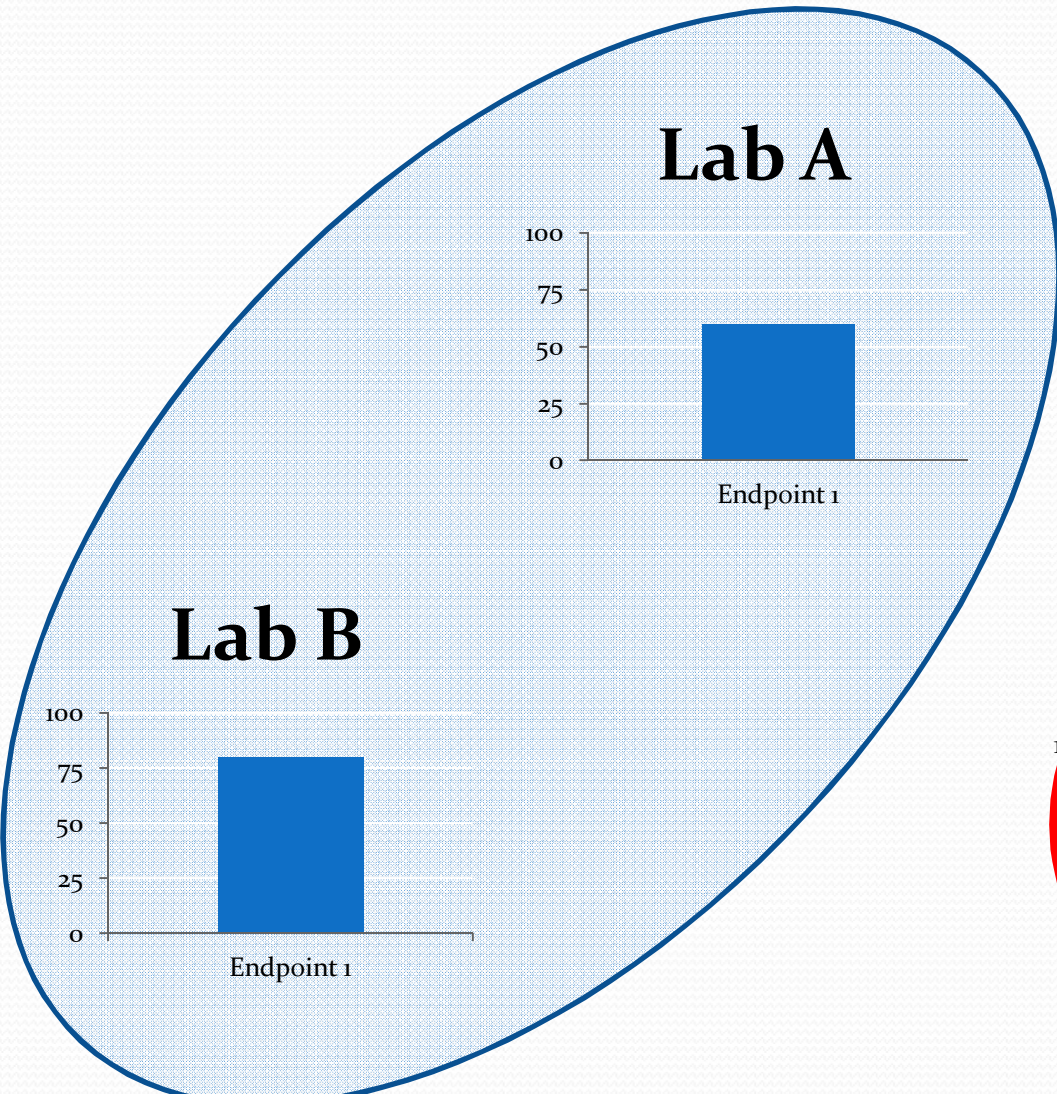
Noldus Satellite Symposium, SfN-11
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Standardization of behavioral phenotyping protocols

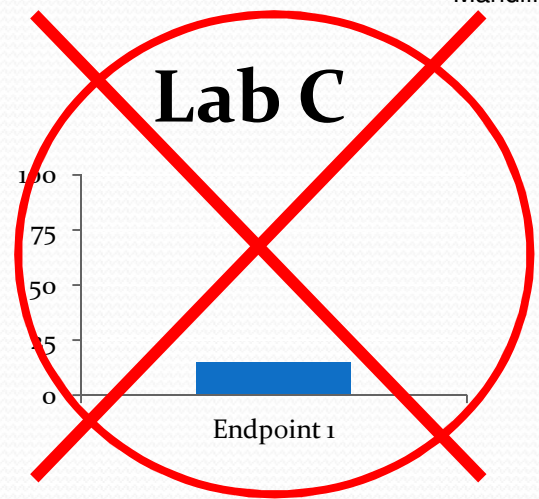
... Equating the laboratory environment does not appear to be feasible. Instead, we need to learn what kinds of behavioral tests yield the most stable results in different labs...

D. Wahlsten, Standardizing tests of mouse behavior: Reasons, recommendations, and reality. 2001.

Standardization



Mandillo et al., 2008





Fallacy of Standardization

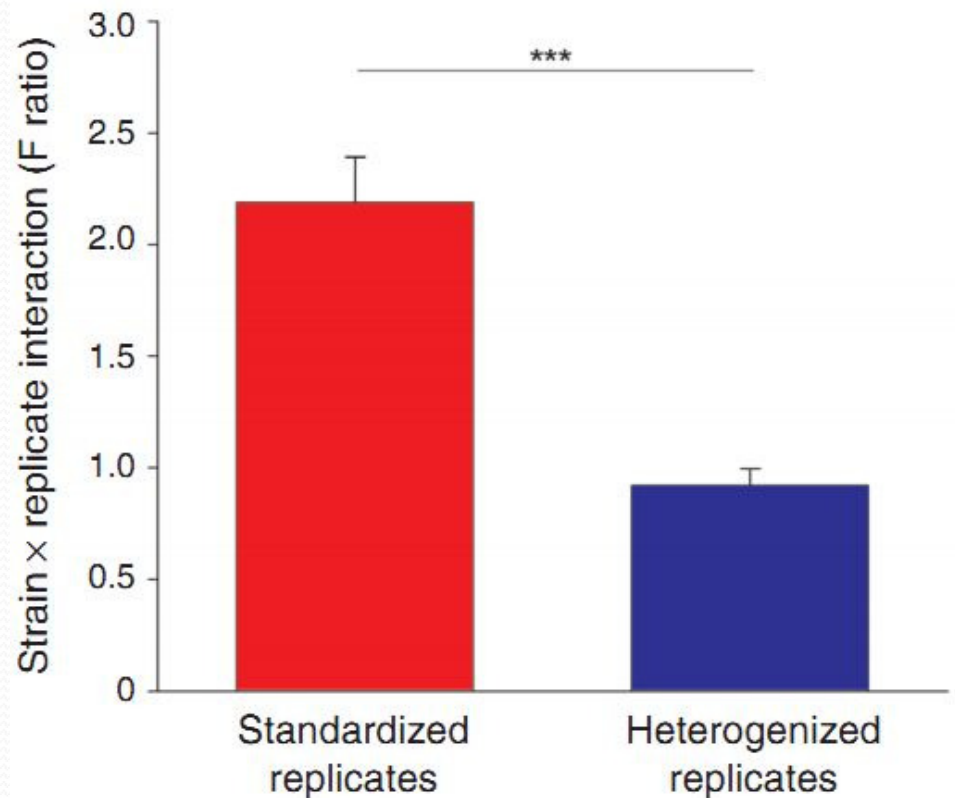
- The different strains, husbandry practices, test protocols, unique procedures might affect the study population and the outcome in different ways and to different degrees.
- Standardization decreases the variability in the experiment to increase the reproducibility of the study.
- Standardization tries to homogenize the study population and decreases the variance.



- If standardization is used to the fully potential, there would be no variation within the study population and the studies would be reproducible all the time.
- The general population is not homogenous, and there is variation.
- Increase in reproducibility at the expense of external validity might have the least translational value.

The variance between replicate experiments

The variance between replicate experiments was significantly greater in standardized replicates compared to heterogenized replicates ($P < 0.001$), indicating that standardization resulted in poorer reproducibility of the results



Environmental standardization: cure or cause of poor reproducibility in animal experiments?

To standardize, or not to standardize?

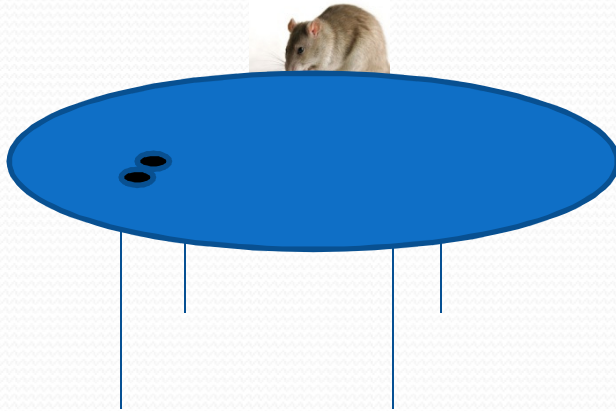


Strategic directions for biopsychiatry research

- New biological concepts
- New biomarkers
- New model organisms
- New behavioral models

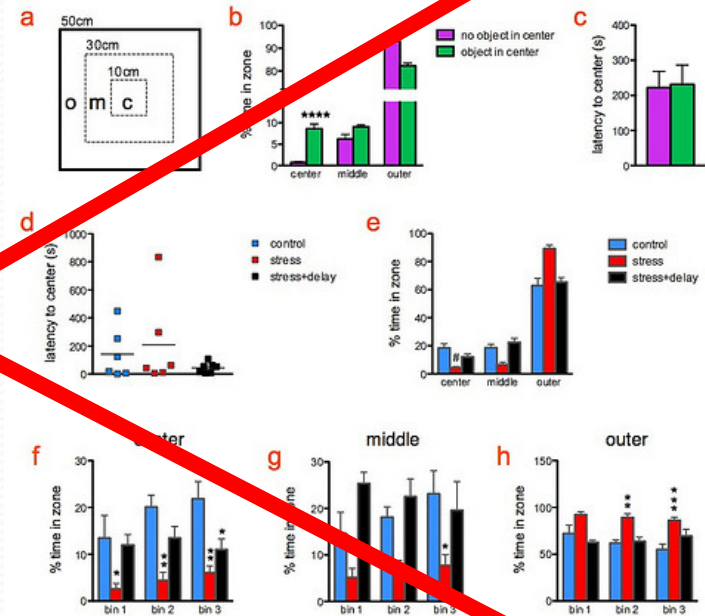
Calvin Hall and the open field test

1. Invented the Open field test to inheritance of emotionality in rats in 1932
2. The field is marked in a grid and square crossings and defecation boli are used to assess the activity of the rodent during first 3 min.



Calvin Hall (1909-1985)

If 100% standardization was implemented in 1932...

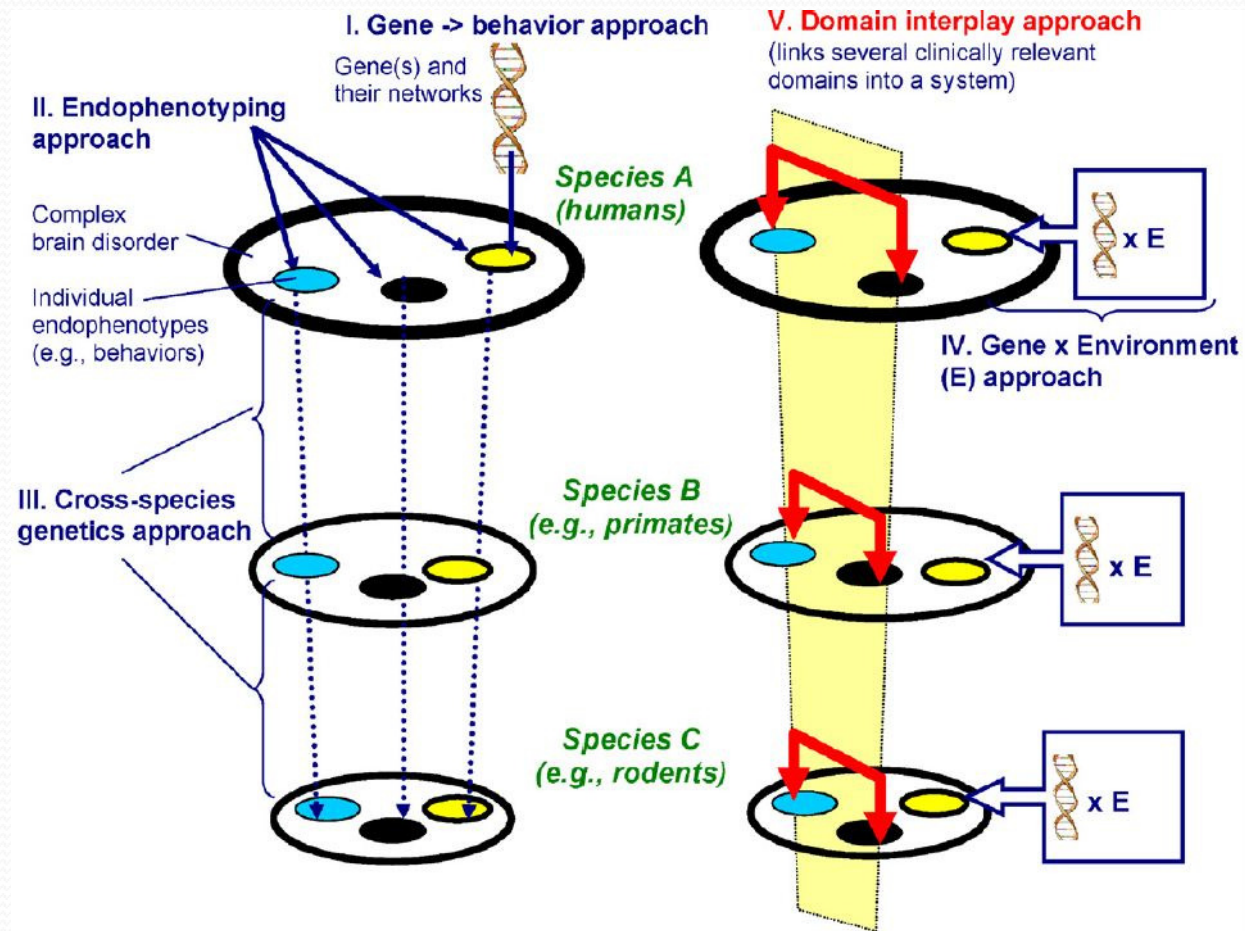




What to do?

- Constant modification and refining of tests, apparatuses, procedures is important
- 100% standardization will stop scientific progress
- Standardization is most needed within a lab - to treat control and experimental groups equally
- **We need to consider the true nature of psychiatric disorders - the interplay (or overlap) between multiple behaviors**

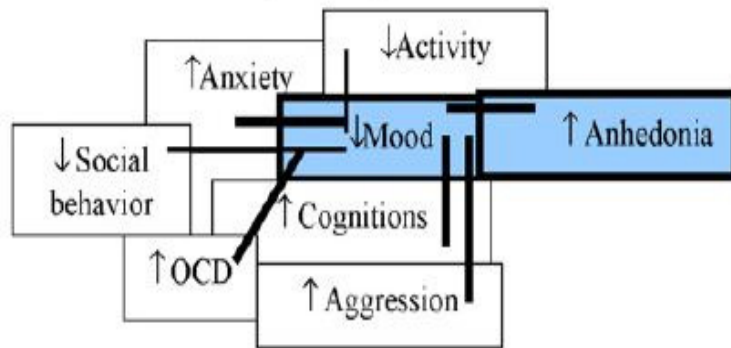
Domain interplay concept of biological psychiatry



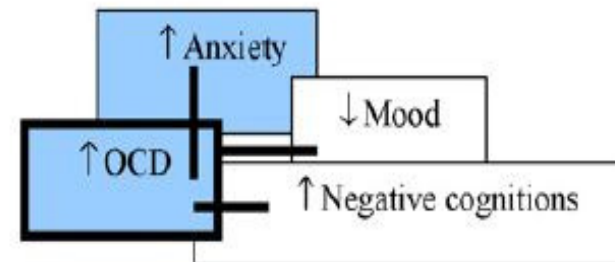
Kalueff et al., 2007, 2009

Behavioral domains interplay in different genetic models

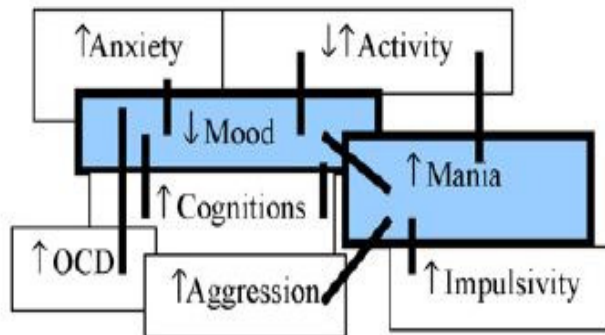
Unipolar depression



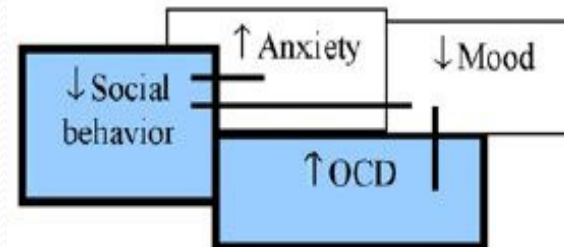
Obsessive-compulsive disorder



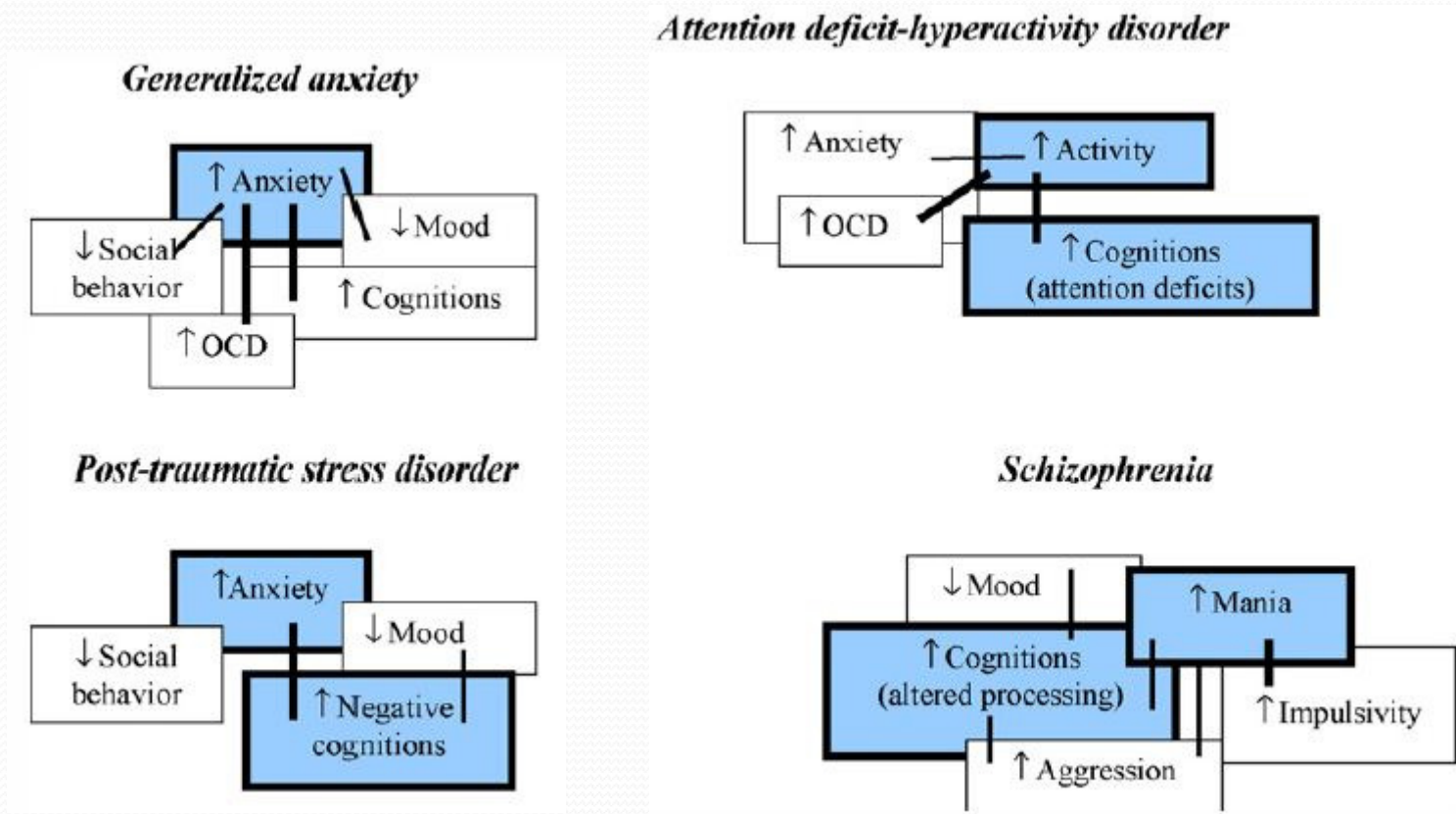
Bipolar depression



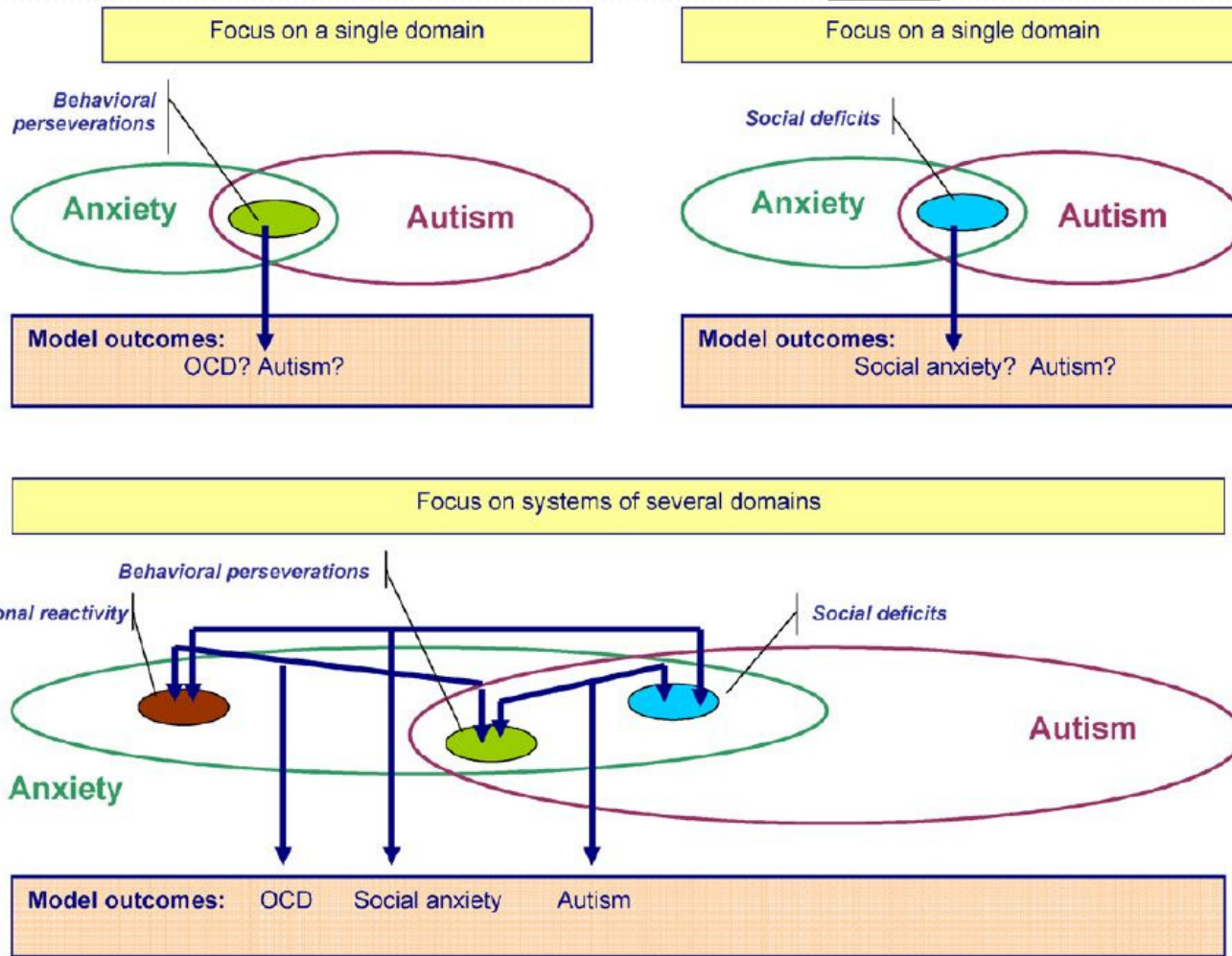
Autism



Behavioral domains interplay in different genetic models

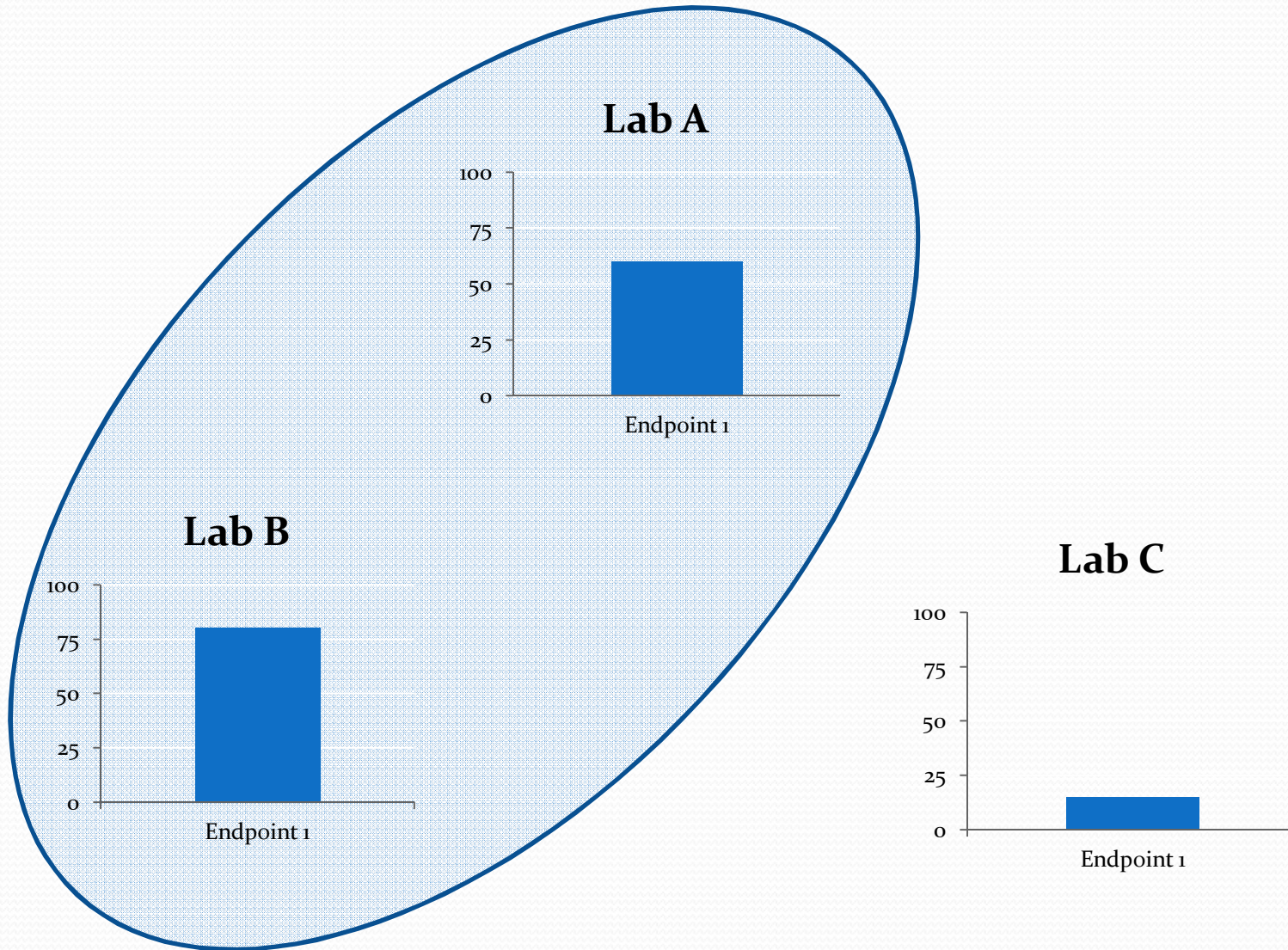


Domain interplay concept in animal models of neuropsychiatric disorders
A new strategy for high-throughput neurophenotyping research

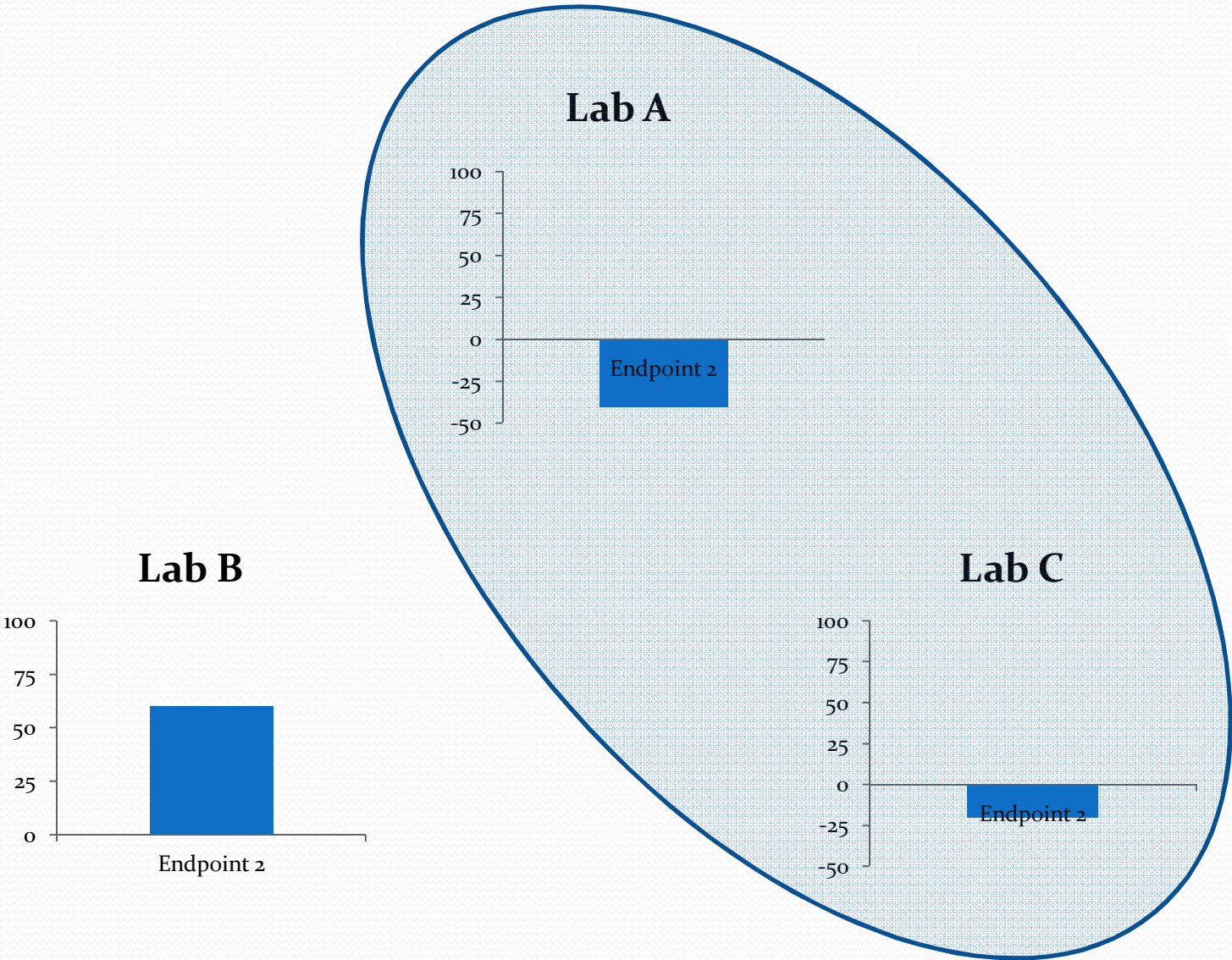


Kalueff et al., 2007, 2009

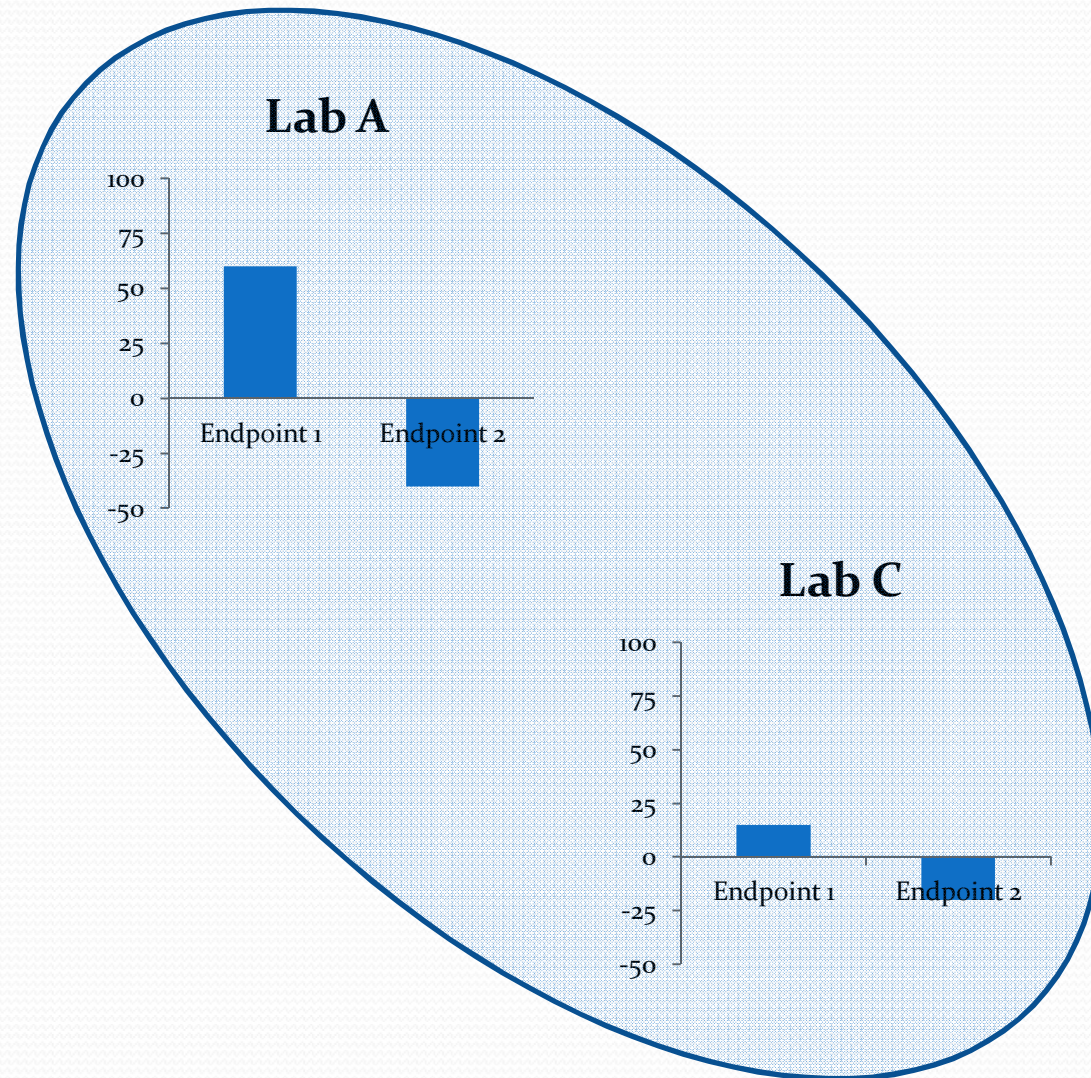
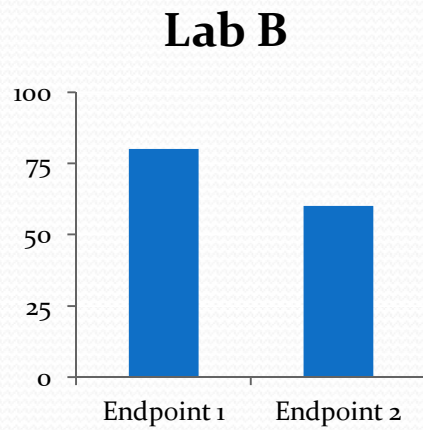
Lab standardization: Behavior A



Lab standardization: Behavior B

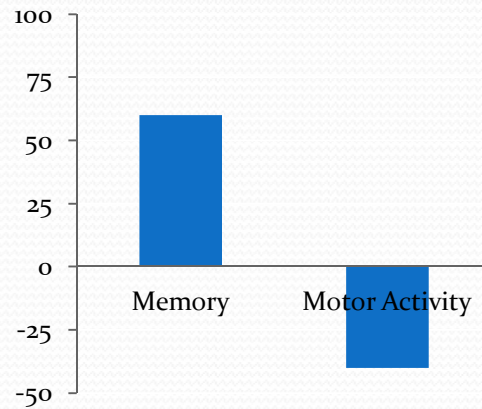


Focus on systems of interlinked phenotypes

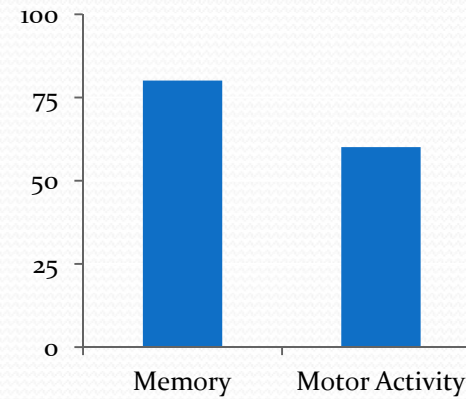


Focus on systems of interlinked phenotypes

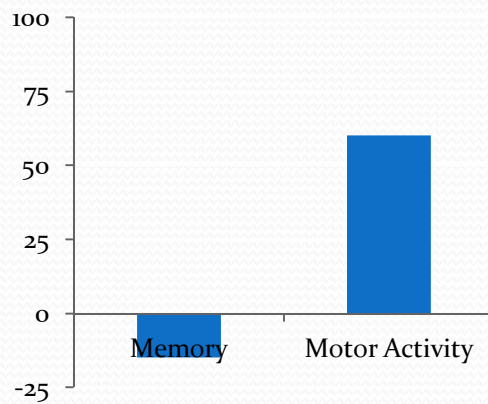
PTSD



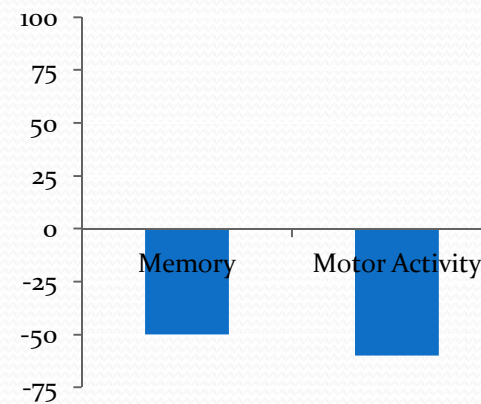
Low stress



ADHD



Parkinsonism





Standardization is important...

- ... when it is applied to experimental groups
- Heterogenization may increase data validity
- We need to constantly refine and improve behavioral phenotyping protocols
- Behavioral phenotyping benefits from assessing systems of interlinked/overlapping phenotypes
- **Focus of such dynamic interplay in animal models better describes the 'real' complex nature of the human disorder in question**
- **Assessing systems of interplaying domains markedly improves our interpretation of animal phenotypes**